FILE 'MEDLINE' ENTERED AT 19:05:26 ON 11 JAN 2005

FILE 'HCAPLUS' ENTERED AT 19:05:26 ON 11 JAN 2005

generic structure

FILE 'BIOSIS' ENTERED AT 19:05:26 ON 11 JAN 2005

FILE 'EMBASE' ENTERED AT 19:05:26 ON 11 JAN 2005

=> s l3 and (multiple(2a)sclero? or demyelinat? or neuropath? or encephalomyeli? or myelopath? or leber? or adrenoleukodystroph? or adrenomyeloneuropath?)
L4 19 L3 AND (MULTIPLE(2A) SCLERO? OR DEMYELINAT? OR NEUROPATH? OR ENCEPHALOMYELI? OR MYELOPATH? OR LEBER? OR ADRENOLEUKODYSTROPH? OR ADRENOMYELONEUROPATH?)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 19 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 abs cbib kwic hitstr 1-19

L5 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted heteroaryl/aryl/cyclo/cycloalkyl/alkyl, naphthyl, quinolinyl, etc.; R2 = (un)substituted -NH-CH2-(CH2)n-CH2-NR4R5, -NH-(CH2)p-phenylene-(CH2)q-NR4R5, -NH(CH2)p-X-R4, etc.; X = pyridinyl; n = 3-8; p = 1-3; q = 0-3; R4, R5 = independently H, amidino, (un)substituted aryl/alkyl; R3 = halo, CN, NO2, aminocarbonyl, (un)substituted alkyl, alkyloxycarbonyl; their tautomers, pharmaceutically acceptable salts, solvates, or amino-protected derivs., with certain compds. excluded] were prepared as inhibitors of protein kinase C (PKC)-theta useful for treating immunol. disorders and type II diabetes. For example, II was prepared in 5 steps via amination of 2,4-dichloro-5-fluoropyrimidine with amine III and 2-chlorobenzylamine. Selected I inhibited PKC-theta with IC50 values ≤ 0.3 μM. Thus, I are useful for treating a disease or disorder associated with T cells activation.

2004:648512 Document Number 141:190795 Preparation of 2,4-diaminopyrimidine derivatives as inhibitors of PKC-theta for treating diseases associated with T cells activation, in particular immunol. disorders and type II diabetes. Cardozo, Mario G.; Cogan, Derek; Cywin, Charles Lawrence; Dahmann, Georg; Disalvo, Darren; Ginn, John David; Prokopowicz, Anthony S.; Spero, Denice M.; Young, Erick Richard Roush (Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim Pharma GmbH & Co. KG). PCT Int. Appl. WO 2004067516 A1 20040812, 124 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR,

BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US2240 20040127. PRIORITY: US 2003-PV443700 20030130.

IT Allergy
Autoimmune disease
Inflammation
Lupus erythematosus
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
(treatment; preparation of diaminopyrimidines as PKC-theta inhibitors for treating diseases associated with T cells activation, in particular immunol. disorders and type II diabetes)

IT 736046-16-5P, Ethyl 4-[[[4-(aminomethyl)cyclohexyl]methyl]amino]-2-[(2-chlorobenzyl)amino]pyrimidine-5-carboxylate 736046-35-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(4-chlorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-40-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(2-methylphenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-45-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(3-methylphenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-49-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(4-methylphenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-53-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(2-fluorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-55-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(3-fluorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-59-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(4-fluorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736046-64-3P, N-(2-Aminobenzyl)-N'-[[4-(aminomethyl)cyclohexyl]methyl]-5-nitropyrimidine-2,4-diamine 736046-69-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3,5-dimethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736046-74-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[3,5-bis(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736046-77-8P, [3-[[[2-[(2-Chlorobenzyl)amino]-5-nitropyrimidin-4-yl]amino]methyl]phenyl]methane amine 736046-80-3P, 2-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]phenol 736046-84-7P, N-(5-Amino-2-chlorobenzyl)-N'-[[4-(aminomethyl)cyclohexyl]methyl]-5-nitropyrimidine-2,4-diamine 736046-89-2P, 4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-2-[(2-chlorobenzyl)amino]pyrimidine-5-carboxamide 736046-94-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chlorobenzyl)-5-fluoropyrimidine-2,4-diamine 736046-98-3P, 3-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]-N-[2-(2-methylphenyl)ethyl]benzamide 736047-11-3P, Methyl 4-[[[4-(aminomethyl)cyclohexyl]methyl]amino]-2-[(2-chlorobenzyl)amino]pyrimidine-5-carboxylate 736047-15-7P, 4-[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]-N-[2-(2-methylphenyl)ethyl]butanamide 736047-19-1P, 5-[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]-N-[2-(2-methylphenyl)ethyl]pentanamide 736047-23-7P, 6-[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]-N-[2-(2-methylphenyl)ethyl]hexanamide 736047-30-6P 736047-34-0P, N-[2-(Methylthio)benzyl]-5-nitro-N'-(piperidin-4-

ylmethyl)pyrimidine-2,4-diamine 736047-39-5P, 5-Nitro-N'-(piperidin-4-ylmethyl)-N-[2-[(trifluoromethyl)thio]benzyl]pyrimidine-2,4-diamine 736047-43-1P, N-(1-Naphthylmethyl)-5-nitro-N'-[(piperidin-4-yl)methyl]pyrimidine-2,4-diamine 736047-48-6P, N'-[[4-[(Dimethylamino)methyl]cyclohexyl]methyl]-N-[2-(methylthio)benzyl]-5-nitropyrimidine-2,4-diamine 736047-52-2P, N'-[[4-[(Dimethylamino)methyl]cyclohexyl]methyl]-5-nitro-N-[2-[(trifluoromethyl)thio]benzyl]pyrimidine-2,4-diamine 736047-57-7P, N'-[[4-[(Dimethylamino)methyl]cyclohexyl]methyl]-N-(1-naphthylmethyl)-5-nitropyrimidine-2,4-diamine 736047-61-3P, N'-[4-[(Dimethylamino)methyl]benzyl]-N-[2-(methylthio)benzyl]-5-nitropyrimidine-2,4-diamine 736047-67-9P, N'-[4-[(Dimethylamino)methyl]benzyl]-5-nitro-N-[2-[(trifluoromethyl)thio]benzyl]pyrimidine-2,4-diamine 736047-72-6P, N'-[4-[(Dimethylamino)methyl]benzyl]-N-(1-naphthylmethyl)-5-nitropyrimidine-2,4-diamine 736047-77-1P, N'-[(1-Methylpiperidin-4-yl)methyl]-N-[2-(methylthio)benzyl]-5-nitropyrimidine-2,4-diamine 736047-82-8P, N'-[(1-Methylpiperidin-4-yl)methyl]-5-nitro-N-[2-[(trifluoromethyl)thio]benzyl]pyrimidine-2,4-diamine 736047-86-2P, N'-[(1-Methylpiperidin-4-yl)methyl]-N-[(1-naphthyl)methyl]-5-nitropyrimidine-2,4-diamine 736047-91-9P, N-(2-Chlorobenzyl)-N'-[(1-methylpiperidin-4-yl)methyl]-5-nitropyrimidine-2,4-diamine 736047-96-4P, N-(2-Methoxybenzyl)-N'-[(1-methylpiperidin-4-yl)methyl]-5-nitropyrimidine-2,4-diamine 736048-02-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-methoxybenzyl)-5-nitropyrimidine-2,4-diamine 736048-08-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-[2-(trifluoromethyl)benzyl]pyrimidine-2,4-diamine 736048-11-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,4-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-16-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-methoxybenzyl)-5-nitropyrimidine-2,4-diamine 736048-21-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[4-fluoro-2-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736048-26-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736048-31-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(pyridin-2-ylmethyl)pyrimidine-2,4-diamine 736048-36-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-40-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-46-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-bromobenzyl)-5-nitropyrimidine-2,4-diamine 736048-52-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,4-dimethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736048-55-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-chloro-5-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736048-60-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,5-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-65-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-[2-(trifluoromethoxy)benzyl]pyrimidine-2,4-diamine 736048-69-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-6-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736048-74-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-79-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-furylmethyl)-5-nitropyrimidine-2,4-diamine 736048-83-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(thien-2-ylmethyl)pyrimidine-2,4-diamine 736048-89-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chlorobenzyl)-5-methylpyrimidine-2,4-diamine 736048-95-6P, N'-(6-Aminohexyl)-N-(2-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736048-99-0P, N-[4-(Aminomethyl)benzyl]-N'-(2-chlorobenzyl)-5-nitropyrimidine-2,4-

diamine 736049-04-0P, N'-(7-Aminoheptyl)-N-(2-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-09-5P, N'-[[3-(Aminomethyl)cyclohexyl]methyl]-N-(2-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-13-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(1-methyl-1-phenylethyl)-5-nitropyrimidine-2,4-diamine 736049-19-7P, 4-(4,4'-Bipiperidin-1-yl)-N-(2-chlorobenzyl)-5-nitropyrimidin-2-amine 736049-25-5P, N-(2-Chlorobenzyl)-N'-[[4-[(dimethylamino)methyl]cyclohexyl]methyl]-5-nitropyrimidin-2,4-diamine 736049-28-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,5-difluorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-34-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[4-(difluoromethoxy)benzyl]-5-nitropyrimidine-2,4-diamine 736049-40-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-ethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736049-49-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736049-55-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-59-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-chloro-2-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-64-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-1-(4-pentylbenzyl)pyrimidine-2,4-diamine 736049-69-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-butoxybenzyl)-5-nitropyrimidine-2,4-diamine 736049-75-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-dimethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736049-79-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,5-dimethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736049-84-6P, N-(2-Chlorobenzyl)-N'-[7-(dimethylamino)heptyl]-5-nitropyrimidine-2,4-diamine 736049-89-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[(1,1'-biphenyl-2-yl)methyl]-5-nitropyrimidine-2,4-diamine 736049-94-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736049-99-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,4-difluorobenzyl)-5-nitropyrimidine-2,4-diamine 736050-04-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-fluoro-4-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736050-10-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-difluorobenzyl)-5-nitropyrimidine-2,4-diamine 736050-14-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(2-chlorobenzyl)pyrimidine-2,4-diamine 736050-19-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,6-dimethoxybenzyl)-5-nitropyrimidine-2,4-diamine 736050-25-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,6-difluorobenzyl)-5-nitropyrimidine-2,4-diamine 736050-28-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-fluoro-3-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736050-34-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-chloro-2-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736050-40-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(1-phenylcyclopropyl)pyrimidine-2,4-diamine 736050-43-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[1-(2-chlorophenyl)-1-methylethyl]-5-nitropyrimidine-2,4-diamine 736050-48-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[(2,3-dihydrobenzo[b]furan-5-yl)methyl]-5-nitropyrimidine-2,4-diamine 736050-53-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[(1,5-dimethyl-1H-pyrrol-2-yl)methyl]-5-nitropyrimidine-2,4-diamine 736050-57-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-bromobenzyl)-5-nitropyrimidine-2,4-diamine 736050-62-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-dimethylbenzyl)-5-nitropyrimidine-2,4-diamine 736050-66-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,4-dimethylbenzyl)-5-nitropyrimidine-2,4-diamine 736050-71-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,5-dimethylbenzyl)-5-nitropyrimidine-

2,4-diamine 736050-76-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-fluoro-5-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736050-86-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-[2-[(trifluoromethyl)thio]benzyl]pyrimidine-2,4-diamine 736050-91-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736050-95-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(6-chloro-2-fluoro-3-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-00-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-6-fluoro-3-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-05-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-naphthyl)-5-nitropyrimidine-2,4-diamine 736051-09-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(1-naphthylmethyl)-5-nitropyrimidine-2,4-diamine 736051-15-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-fluoro-4-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736051-20-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-chloro-2-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-26-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(5-chloro-2-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-29-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3-chloro-2-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-34-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[5-fluoro-2-(trifluoromethyl)benzyl]-5-nitropyrimidine-2,4-diamine 736051-40-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(5-chloro-2-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736051-44-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-difluoro-4-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-49-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(5-fluoro-2-methylbenzyl)-5-nitropyrimidine-2,4-diamine 736051-54-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(1-naphthyl)-5-nitropyrimidine-2,4-diamine 736051-58-4P, [4-trans-[[[2-[(2-Chlorobenzyl)amino]-5-nitropyrimidin-4-yl]amino]methyl]cyclohexyl]methanol 736051-63-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(2,5-dichlorobenzyl)pyrimidine-2,4-diamine 736051-68-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(2,4-dichlorobenzyl)pyrimidine-2,4-diamine 736051-73-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(2-bromobenzyl)pyrimidine-2,4-diamine 736051-78-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(cyclohexylmethyl)-5-nitropyrimidine-2,4-diamine 736051-83-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-naphthylmethyl)-5-nitropyrimidine-2,4-diamine 736051-87-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-[2-(trifluoromethoxy)benzyl]pyrimidine-2,4-diamine 736051-92-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-[2-(trifluoromethyl)benzyl]pyrimidine-2,4-diamine 736051-95-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(difluoromethoxy)benzyl]-5-nitropyrimidine-2,4-diamine 736052-01-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[3-(difluoromethoxy)benzyl]-5-nitropyrimidine-2,4-diamine 736052-06-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-4-fluorobenzyl)-5-nitropyrimidine-2,4-diamine 736052-12-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-3,6-difluorobenzyl)-5-nitropyrimidine-2,4-diamine 736052-16-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(2,3,5-trifluorobenzyl)pyrimidine-2,4-diamine 736052-21-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(2,3,4,5-tetrafluorobenzyl)pyrimidine-2,4-diamine 736052-30-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-dihydro-1H-inden-2-yl)-5-

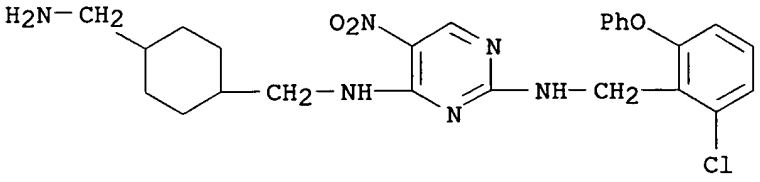
nitropyrimidine-2,4-diamine 736052-41-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-chloro-1-naphthyl)-5-nitropyrimidine-2,4-diamine 736052-46-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(4-methoxy-2-naphthyl)-5-nitropyrimidine-2,4-diamine 736052-50-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-quinolin-6-ylpyrimidine-2,4-diamine 736052-54-3P, N'-[[4-trans-(Aminomethyl)cyclohexyl]methyl]-N-(2,5-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736052-58-7P, N'-[[4-trans-(Aminomethyl)cyclohexyl]methyl]-N-(2,3-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736052-63-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(2-chlorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736052-68-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(3-chlorophenyl)ethyl]-5-nitropyrimidine-2,4-diamine **736052-71-4P**, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-6-phenoxybenzyl)-5-nitropyrimidine-2,4-diamine 736052-76-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(2-naphthyl)pyrimidine-2,4-diamine 736052-81-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-bromo-N-(1-naphthylmethyl)pyrimidine-2,4-diamine 736052-86-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(pyridin-3-ylmethyl)pyrimidine-2,4-diamine 736052-90-7P, 4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-2-[(2-chlorobenzyl)amino]pyrimidine-5-carbonitrile 736052-95-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[4-(dimethylamino)benzyl]-5-nitropyrimidine-2,4-diamine 736053-00-2P, N'-[[4-trans-(Aminomethyl)cyclohexyl]methyl]-N-(2-bromobenzyl)-5-nitropyrimidine-2,4-diamine 736053-06-8P, N'-(7-Aminoheptyl)-N-(2-bromobenzyl)-5-nitropyrimidine-2,4-diamine 736053-12-6P, N'-(7-Aminoheptyl)-N-(2,5-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736053-16-0P, N-[[4-[[[2-[(2-Chlorobenzyl)amino]-5-nitropyrimidin-4-yl]amino]methyl]cyclohexyl]methyl]guanidine 736053-22-8P, N-(3-Aminobenzyl)-N'-[[4-(aminomethyl)cyclohexyl]methyl]-5-nitropyrimidine-2,4-diamine 736053-28-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(2-nitrobenzyl)pyrimidine-2,4-diamine 736053-35-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(2-bromophenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736053-41-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-bromobenzyl)-5-chloropyrimidine-2,4-diamine 736053-45-5P, [4-[[[2-[[2-(1H-Indol-3-yl)ethyl]amino]-5-nitropyrimidin-4-yl]amino]methyl]cyclohexyl]methanaminium chloride 736053-50-2P, N-[[3-[[[2-[(2-Chlorobenzyl)amino]-5-nitropyrimidin-4-yl]amino]methyl]cyclohexyl]methyl]guanidine 736053-55-7P, 3-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]phenol 736053-62-6P, [4-[[[2-[[2-(1H-Imidazol-4-yl)ethyl]amino]-5-nitropyrimidin-4-yl]amino]methyl]cyclohexyl]methanaminium chloride 736053-66-0P, N-(2-Chlorobenzyl)-N'-[[4-cis-[(dimethylamino)methyl]cyclohexyl]methyl]-5-nitropyrimidine-2,4-diamine 736053-70-6P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-chloro-N-(2-chlorobenzyl)pyrimidine-2,4-diamine 736053-76-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(2-phenylethyl)pyrimidine-2,4-diamine 736053-81-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(3-phenylpropyl)pyrimidine-2,4-diamine 736053-86-4P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(4-phenylbutyl)pyrimidine-2,4-diamine 736053-92-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(2-phenylpropyl)pyrimidine-2,4-diamine 736053-95-5P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(4-methoxyphenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736053-99-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(3-methoxyphenyl)ethyl]-5-nitropyrimidine-2,4-diamine 736054-02-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-[2-(2-methoxyphenyl)ethyl]-5-

nitropyrimidine-2,4-diamine 736054-07-2P, 4-[[[2-[(2-Chlorobenzyl)amino]-5-nitropyrimidin-4-yl]amino]methyl]piperidine-1-carboximidamide 736054-12-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(3,5-dichlorobenzyl)-5-nitropyrimidine-2,4-diamine 736054-43-6P, 4-[[(4-Aminomethylcyclohexyl)methyl]amino]-2-(2-chlorobenzylamino)pyrimidine-5-carboxylic acid 736055-49-5P, N'-[4-(Aminomethyl)benzyl]-N-(2-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736055-53-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-(4-pentylbenzyl)pyrimidine-2,4-diamine 736055-72-4P, N'-(5-Aminopentyl)-N-(2-chlorobenzyl)-5-nitropyrimidine-2,4-diamine 736055-76-8P, 2-(Benzylamino)-4-(1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl)-5-trifluoromethylpyrimidine 736055-82-6P, 2-(4-Chlorobenzylamino)-4-(1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl)-5-nitropyrimidine 736055-87-1P, 2-(2-Chlorobenzylamino)-4-(1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl)-5-nitropyrimidine 736055-90-6P, 2-Benzylamino-4-(1,4,6,7-tetrahydroimidazo[4,5-c]pyridin-5-yl)-5-nitropyrimidine 737756-40-0P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-((2R)-1,2,3,4-tetrahydronaphthalen-2-yl)pyrimidine-2,4-diamine 737756-41-1P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-((2S)-1,2,3,4-tetrahydronaphthalen-2-yl)pyrimidine-2,4-diamine 737756-42-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-((1R)-1,2,3,4-tetrahydronaphthalen-1-yl)pyrimidine-2,4-diamine 737756-43-3P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-((1S)-1,2,3,4-tetrahydronaphthalen-1-yl)pyrimidine-2,4-diamine 737756-44-4P, (1S,2R)-2-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]cyclohexanol 737756-45-5P, (1R,2R)-2-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]cyclohexanol 737756-46-6P, (1R,3R)-3-[[[4-[[[4-(Aminomethyl)cyclohexyl]methyl]amino]-5-nitropyrimidin-2-yl]amino]methyl]-4,4-dimethylcyclohexanol 737756-47-7P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-[(1S)-1-(phenyl)ethyl]pyrimidine-2,4-diamine 737756-48-8P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-5-nitro-N-[(1R)-1-(phenyl)ethyl]pyrimidine-2,4-diamine 737756-49-9P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-((1S)-2,3-dihydro-1H-inden-1-yl)-5-nitropyrimidine-2,4-diamine 737756-50-2P, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-((1R)-2,3-dihydro-1H-inden-1-yl)-5-nitropyrimidine-2,4-diamine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PKC-theta inhibitor; preparation of diaminopyrimidines as PKC-theta inhibitors for treating diseases associated with T cells activation, in particular immunol. disorders and type II diabetes)

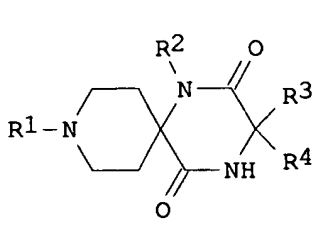
IT **736052-71-4P**, N'-[[4-(Aminomethyl)cyclohexyl]methyl]-N-(2-chloro-6-phenoxybenzyl)-5-nitropyrimidine-2,4-diamine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PKC-theta inhibitor; preparation of diaminopyrimidines as PKC-theta inhibitors for treating diseases associated with T cells activation, in particular immunol. disorders and type II diabetes)

RN 736052-71-4 HCAPLUS

CN 2,4-Pyrimidinediamine, N4-[[4-(aminomethyl)cyclohexyl]methyl]-N2-[(2-chloro-6-phenoxyphenyl)methyl]-5-nitro- (9CI) (CA INDEX NAME)



L5 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



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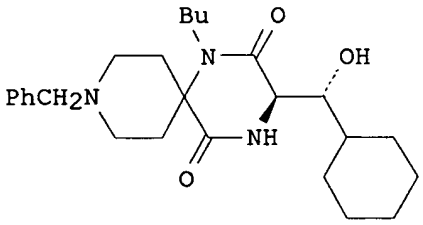

II

AB The title compds. [I; R1 = (a) each (un)substituted and partially or completely saturated C3-15 mono-, di-, or tricarbocyclic aryl or 3- to 15-membered mono-, di-, or triheterocyclic aryl latter containing heteroatoms selected from 1-4 N atoms, 1 or 2 O atoms, and/or 1 or 2 S atoms, or (b) C1-8 alkyl, C2-4 alkenyl, or C2-4 alkynyl each substituted by 1-3 substituents selected from each (un)substituted HO, acyl, NH2, CONH2, acylamino, sulfonylamino, :NH, and :NOH; R2 = H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, each (un)substituted Ph, pyridinyl, or C3-8 cycloalkyl, group (b); R3, R4 = (i) H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, or (ii) C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl each substituted by 1-5 substituents selected from group (a), HO, and tetrahydropyran-4-ylidene], quaternary ammonium salts, N-oxides, or salts thereof are prepared These compds. are useful in preventing and/or treating various inflammatory diseases (asthma, nephritis, nephropathy, hepatitis, arthritis, rheumatoid arthritis, rhinitis, conjunctivitis, ulcerative colitis, etc.), immune diseases (autoimmune disease, transplant rejection, immune suppression, psoriasis, **multiple sclerosis**, etc.), infection with human immunodeficiency virus (acquired immune deficiency syndrome), allergic diseases (atopic dermatitis, urticaria, allergic bronchopulmonary aspergillosis, allergic eosinophilic gastroenteritis, etc.), ischemic reperfusion injury, acute respiratory distress syndrome, shock accompanying bacterial infection, diabetes, cancer metastasis, etc. (no data). They are improved in bioavailability when administered orally, metabolic stability, liver or systemic clearance, or affinity for chemokine receptor CCR compared to prior art compds. and exhibit very low toxicity. Thus, 1-benzyl-4-piperidone, (2R,3R)-2-(tert-butoxycarbonylamino)-3-cyclohexyl-3-hydroxypropanoic acid, n-butylamine, and 2-(morpholin-4-yl)ethyl isocyanide were stirred in MeOH at 50° overnight to give, after workup, 1-benzyl-4-[2-(morpholin-4-yl)ethylaminocarbonyl]-4-[N-butyl-N-[(2R,3R)-2-amino-3-hydroxy-3-cyclohexylpropanoyl]amino]piperidine which was stirred in AcOH at 70° for 1 h to give, after workup, (3R)-1-butyl-2,5-dioxo-3-[(1R)-1-hydroxy-1-cyclohexylmethyl]-9-phenylmethyl-1,4,9-triazaspiro[5.5]undecane

(II). A tablet and an ampule formulation containing specific compound I were described.

2004:267336 Document Number 140:303699 Preparation of triazaspiro[5.5]undecane derivatives as chemokine receptor CCR5 antagonists and drugs comprising the same as the active ingredients. Takaoka, Yoshikazu; Nishizawa, Rena; Shibayama, Shiro; Sagawa, Kenji; Matsuo, Masayoshi (Ono Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 2004026873 A1 20040401, 288 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP11834 20030917. PRIORITY: JP 2002-270849 20020918.

AB . . . nephritis, nephropathy, hepatitis, arthritis, rheumatoid arthritis, rhinitis, conjunctivitis, ulcerative colitis, etc.), immune diseases (autoimmune disease, transplant rejection, immune suppression, psoriasis, **multiple sclerosis**, etc.), infection with human immunodeficiency virus (acquired immune deficiency syndrome), allergic diseases (atopic dermatitis, urticaria, allergic bronchopulmonary aspergillosis, allergic eosinophilic. . .

IT Allergy
Allergy inhibitors
Anti-AIDS agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antirheumatic agents
Antiviral agents
Arthritis
Asthma
Autoimmune disease
Diabetes mellitus
Hepatitis
Human
Human immunodeficiency virus 1
Immunosuppression
Inflammation
Kidney, disease
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
Transplant rejection
Urticaria
(preparation of triazaspiro[5.5]undecane derivs. as chemokine receptor CCR5 antagonists and drugs)

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676454-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triazaspiro[5.5]undecane derivs. as chemokine receptor CCR5 antagonists and drugs)

IT **676454-13-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triazaspiro[5.5]undecane derivs. as chemokine receptor CCR5 antagonists and drugs)

RN 676454-13-0 HCAPLUS

CN Benzamide, 2-[4-[[(3R)-1-butyl-3-[(R)-3-cyclopenten-1-ylhydroxymethyl]-2,5-dioxo-1,4,9-triazaspiro[5.5]undec-9-yl]methyl]phenoxy]-N-[2-(dimethylamino)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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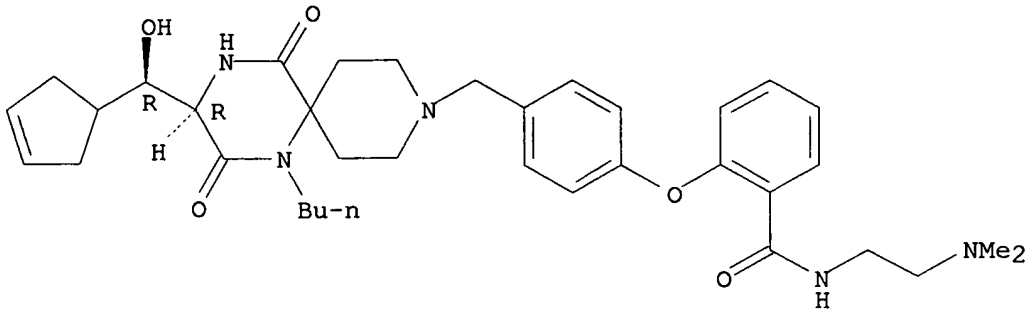

●2 HCl

L5 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
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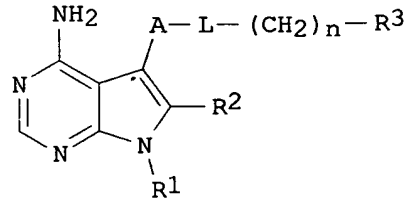

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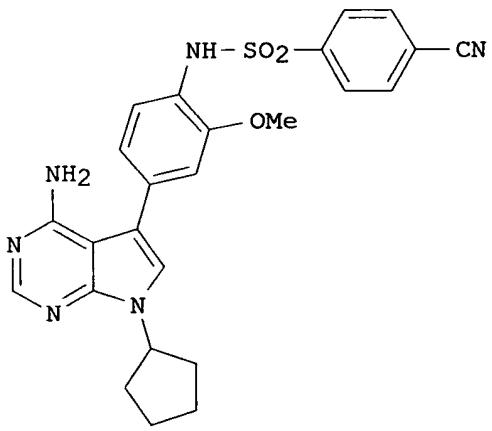

II

AB 7H-Pyrrolo[2,3-d]pyrimidin-4-amines [I; A = (un)substituted 6-membered aromatic ring or 5- or 6-membered heteroarom. ring; L = RbNRSO2, RbNRP(O), or RbNRP(O)O, where Rb = alkylene group which when taken together with the sulfonamide, phosphinamide or phosphonamide group to which it is bound forms a 5- or 6-membered ring fused to ring A, or L = O, S, NR, 5-7 membered (oxa)azaphosphaarom. or (oxa)azaphosphacycloalkyl ring, or a

variety of linkers containing functional groups; R = H, acyl, or (un)substituted aliphatic, (hetero)aromatic, or cycloalkyl; R1 = H, 2-Ph-1,3-dioxan-5-yl or (un)substituted (cyclo)alkyl, cycloalkenyl, or phenylalkyl; R2 = H, halo, OH, CN, (un)substituted aliphatic, cycloalkyl, (hetero)aromatic, (hetero)aralkyl, amino, or amido; R3 = (un)substituted aliphatic, alkenyl, (hetero)cycloalkyl, or (hetero)aromatic; n = 0-6], and physiol. acceptable salts and metabolites thereof, were prepared For example, II was prepared in a 6-step sequence involving: (1) amine protection of 4-bromo-2-methoxyaniline with di-tert-Bu dicarbonate, (2) 4-addition of diboron pinacol ester, (3) 4-substitution with 4-chloro-7-cyclopentyl-5-iodo-7H-pyrrolo[2,3-d]pyrimidine, (4) deprotection of the amine with F3CCO2H, (5) 4-amination of the pyrrolopyrimidine, and (6) amidation of the aniline with 4-cyanobenzenesulfonyl chloride. I inhibit serine/threonine and tyrosine kinase activity, affecting immunol., hyperproliferative, and angiogenic processes. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at concns. of ≤ 50 μM, and some significantly inhibited cdc2 at concns. of 50 ≤ μM. Thus, these compds. are useful in the treatment of cancer and hyperproliferative disorders, rheumatoid arthritis, disorders of the immune system, transplant rejections, and inflammatory disorders.

2003:777394 Document Number 139:292260 Preparation of 4-aminopyrrolopyrimidines as protein kinase inhibitors. Calderwood, David; Arnold, Lee; Mazdiyasni, Hormoz; Hirst, Gavin C.; Deng, Bojuan B.; Johnston, David N.; Rafferty, Paul; Tometzki, Gerald B.; Twigger, Helen L.; Munschauer, Rainer (USA). U.S. Pat. Appl. Publ. US 2003187001 A1 20031002, 93 pp., Cont.-in-part of U.S. 6,001,839. (English). CODEN: USXXCO. APPLICATION: US 1999-399083 19990917. PRIORITY: US 1998-42702 19980317; US 1998-PV100954 19980918.

IT Ascites
Asthma
Atherosclerosis
Cirrhosis
Exudate
Fibrosis
Glaucoma (disease)
Hodgkin's disease
Leukemia
Lyme disease
Lymphoma
Melanoma
Multiple myeloma
Multiple sclerosis
Osteoarthritis
Preeclampsia
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sarcoma
Sepsis
Transplant rejection
(treatment of; preparation of 7H-pyrrolo[2,3-d]pyrimidin-4-amines for inhibiting protein kinase activity)

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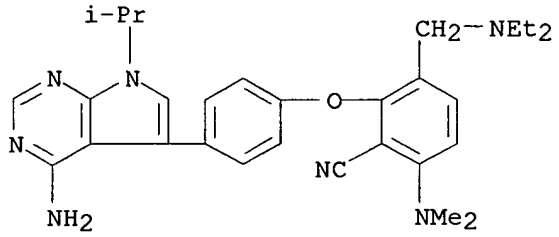
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of 7H-pyrrolo[2,3-d]pyrimidin-4-amines as protein kinase inhibitors)

IT **262431-43-6P 262431-44-7P 262431-45-8P**
262431-46-9P 262431-47-0P 262431-50-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of 7H-pyrrolo[2,3-d]pyrimidin-4-amines as protein kinase inhibitors)

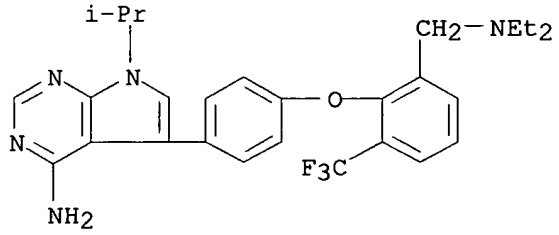
RN 262431-43-6 HCAPLUS

CN Benzonitrile, 2-[4-[4-amino-7-(1-methylethyl)-7H-pyrrolo[2,3-d]pyrimidin-5-

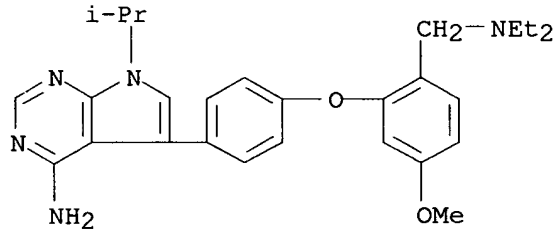
yl]phenoxy]-3-[(diethylamino)methyl]-6-(dimethylamino)- (9CI) (CA INDEX NAME)



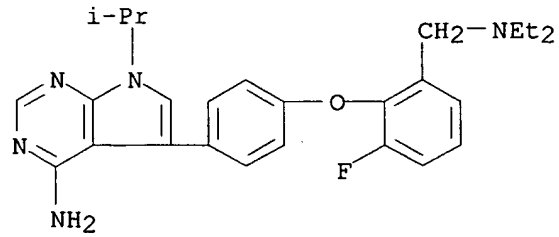
RN 262431-44-7 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]-6-(trifluoromethyl)phenoxy]phenyl]-7-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 262431-45-8 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]-5-methoxyphenoxy]phenyl]-7-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 262431-46-9 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]-6-fluorophenoxy]phenyl]-7-(1-methylethyl)- (9CI) (CA INDEX NAME)



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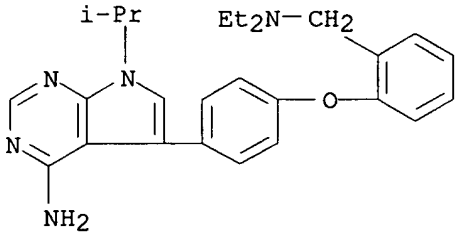
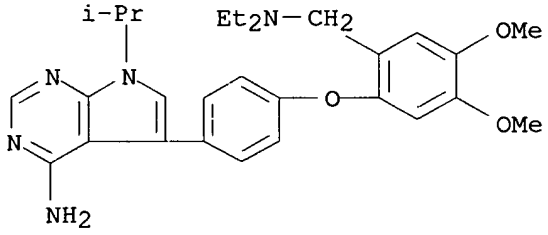
RN 262431-47-0 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]phenoxy]phenyl]-7-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 262431-50-5 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]-4,5-dimethoxyphenoxy]phenyl]-7-(1-methylethyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
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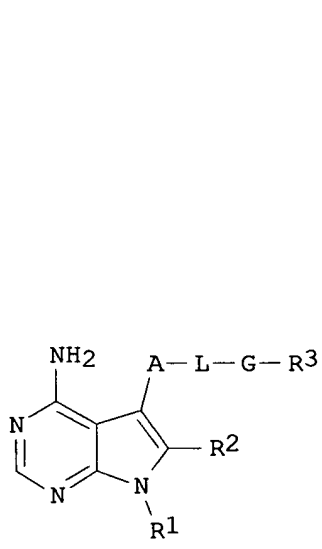

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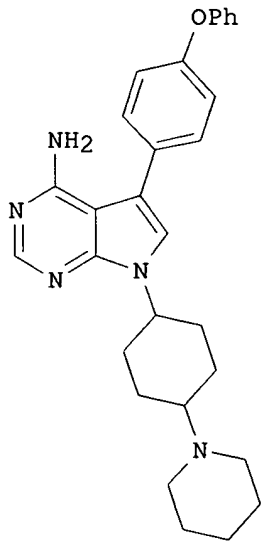

II

AB The title compds. I [A = (un)substituted 6-membered aromatic ring, 5-6 membered heteroarom. ring; L = O, S, SO, SO2, etc.; G = a direct bond, (CH2)j (wherein j = 1-6), alkenylene, cycloalkylene, oxaalkylene; R1 = alkyl, cycloalkyl, bicycloalkyl, etc.; R2 = H, alkyl, cycloalkyl, halo, etc.; R3 = alkyl, alkenyl, cycloalkyl, etc.] and physiol. acceptable salts and metabolites thereof, are inhibitors of serine/threonine and tyrosine kinase activity. Several of the kinases, whose activity is inhibited by compds. I, are involved in immunol., hyperproliferative, or angiogenic processes. Thus, the compds. I can ameliorate disease states where angiogenesis or endothelial cell hyperproliferation is a factor. These compds. can be used to treat cancer and hyperproliferative disorders, rheumatoid arthritis, disorders of the immune system, transplant rejections and inflammatory disorders. All exemplified compds. I significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at ≤50 μM, and some significantly inhibited cdc2 at ≤50 μM. 546 Example prepns. are included. For example, addition of piperidine to 4-[4-amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]cyclohexanone in DCE and AcOH, followed by treatment with Na[(AcO)3BH], workup and chromatog., gave cis- and trans-II.

2003:633320 Document Number 139:180075 Preparation of pyrrolopyrimidines as tyrosine kinase inhibitors. Hirst, Gavin C.; Calderwood, David; Munschauer, Rainer; Arnold, Lee D.; Johnston, David N.; Rafferty, Paul (Abbott GmbH & Co. KG, USA). U.S. Pat. Appl. Publ. US 2003153752 A1 20030814, 166 pp., Cont.-in-part of Appl. Number PCT/US99/21560. (English). CODEN: USXXCO. APPLICATION: US 2000-537167 20000329. PRIORITY: US 1998-PV100832 19980918; US 1998-PV100833 19980918; US 1998-PV100834 19980918; US 1998-PV100946 19980918; WO 1999-US21560 19990917.

IT Anemia (disease)
Atherosclerosis
Cirrhosis
Fibrosis
Glaucoma (disease)
Hodgkin's disease
Ischemia
Leukemia
Lyme disease
Lymphoma
Melanoma
Multiple myeloma
Multiple sclerosis
Necrosis
Osteoarthritis
Preeclampsia
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sarcoma
Sickle cell anemia
Transplant rejection
Wound
(treatment; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 262442-50-2P 262442-56-8P 262442-76-2P 262442-90-0P 364353-91-3P
364353-94-6P 364353-96-8P 364354-00-7P 364354-01-8P
364354-05-2P 364354-08-5P 364354-14-3P 364354-16-5P 364354-17-6P
364354-19-8P 364354-21-2P 364354-26-7P 364354-27-8P 364354-28-9P

364354-30-3P 364354-32-5P 364354-34-7P 364354-36-9P 364354-39-2P
364354-40-5P 364354-41-6P 364354-42-7P 364354-43-8P 364354-44-9P
364354-45-0P 364354-46-1P 364354-47-2P 364354-48-3P 364354-51-8P
364354-52-9P 364354-53-0P 364354-54-1P 364354-55-2P 364354-56-3P
364354-57-4P 364354-59-6P 364354-60-9P 364354-61-0P 364354-62-1P
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364354-74-5P 364354-75-6P 364354-80-3P 364354-81-4P 364354-85-8P
364354-86-9P 364354-90-5P 364354-94-9P 364354-95-0P 364354-97-2P,
Cis-4-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-[2-[(1H-imidazol-2-ylmethyl)amino]ethyl]-1-cyclohexanol diacetate
364354-98-3P 364354-99-4P 364355-00-0P 364355-01-1P 364355-02-2P
364355-03-3P 364355-04-4P 364355-06-6P, Trans-1-(Aminomethyl)-4-[4-amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-cyclohexanol diacetate 364355-07-7P 364355-08-8P 364355-09-9P 364355-10-2P
364355-11-3P 364355-12-4P 364355-13-5P 364355-14-6P 364355-15-7P
364355-16-8P 364355-18-0P 364355-19-1P 364355-20-4P 364355-21-5P
364355-22-6P 364355-23-7P 364355-24-8P 364355-25-9P 364355-27-1P,
Cis-8-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1,3-diazaspiro[4.5]decan-2-one 364355-29-3P, Cis-4-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-ammoniocyclohexylmethanol acetate 364355-33-9P 364355-35-1P
364355-38-4P, 5-[4-(Benzyloxy)phenyl]-7-(1,4-dioxaspiro[4.5]dec-8-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine 364355-40-8P 364355-41-9P
364355-44-2P 364355-51-1P 364355-53-3P 364355-56-6P 364355-57-7P
364355-58-8P 364355-59-9P 364355-60-2P 364355-62-4P 364355-63-5P
364355-64-6P 364355-65-7P 364355-66-8P 364355-68-0P 364355-71-5P
364355-75-9P 364355-76-0P 364355-77-1P 364355-78-2P 364355-79-3P
364355-80-6P 364355-81-7P 364355-82-8P 364355-83-9P 364355-84-0P
364355-85-1P 364355-86-2P 364355-87-3P 364355-88-4P 364355-89-5P
364355-90-8P 364355-91-9P 364355-92-0P 364355-93-1P 364355-96-4P
364355-97-5P 364356-05-8P 364356-08-1P 364356-11-6P 364356-13-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 62-53-3, Aniline, reactions 75-64-9, tert-Butylamine, reactions 77-86-1 78-96-6, 1-Amino-2-propanol 79-30-1, Isobutyryl chloride 96-20-8, 2-Amino-1-butanol 98-09-9, Benzenesulfonyl chloride 98-80-6, Phenylboronic acid 100-36-7, N,N-Diethylethylenediamine 100-52-7, Benzaldehyde, reactions 100-55-0, 3-Pyridylmethanol 103-71-9, Phenyl isocyanate, reactions 103-80-0, Phenacetyl chloride 104-78-9, 3-Diethylaminopropylamine 105-36-2, Ethyl bromoacetate 105-83-9 108-00-9, N,N-Dimethylethylenediamine 108-15-6, 1-Dimethylamino-2-propylamine 109-01-3, N-Methylpiperazine 109-02-4, 4-Methylmorpholine 109-55-7 109-85-3, 2-Methoxyethylamine 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 115-69-5, 2-Amino-2-methyl-1,3-propanediol 120-29-6, Tropine 120-43-4, Ethyl 1-piperazinecarboxylate 121-05-1, N,N-Diisopropylethylenediamine 123-00-2, 4-(3-Aminopropyl)morpholine 123-75-1, Pyrrolidine, reactions 124-68-5 140-31-8, 2-(Piperazin-1-yl)ethylamine 142-25-6, N,N,N'-Trimethylethylenediamine 156-87-6, 3-Amino-1-propanol 285-69-8, 3,6-Dioxabicyclo[3.1.0]hexane 288-32-4, Imidazole, reactions 349-88-2, 4-Fluorobenzenesulfonyl chloride 364-73-8, 5-Bromo-2-fluoronitrobenzene 367-24-8, 4-Bromo-2-fluoroaniline 446-52-6, 2-Fluorobenzaldehyde 453-20-3, Tetrahydro-3-furanol 501-53-1, Benzyl chloroformate 535-11-5, Ethyl 2-bromopropionate 540-38-5, 4-Iodophenol 574-98-1

586-95-8, 4-Pyridylmethanol 586-98-1, 2-Pyridylmethanol 615-18-9, 2-Chlorobenzoxazole 616-30-8, 3-Amino-1,2-propanediol 622-40-2, 2-Morpholinoethanol 623-04-1, 4-Aminobenzyl alcohol 645-45-4, Hydrocinnamoyl chloride 929-06-6, 2-(2-Aminoethoxy)ethanol 1445-73-4, 1-Methylpiperid-4-one 1765-93-1, 4-Fluorophenylboronic acid 1878-68-8, 4-Bromophenylacetic acid 1885-14-9, Phenyl chloroformate 2038-03-1, 4-(2-Aminoethyl)morpholine 2081-44-9, Tetrahydro-2H-4-pyranol 2105-94-4, 4-Bromo-2-fluorophenol 2295-31-0, 2,4-Thiazolidinedione 2362-12-1, 4-Bromo-2-methylphenol 2706-56-1, 2-(2-Aminoethyl)pyridine 2749-11-3, (S)-(+)-2-Amino-1-propanol 2799-16-8 2799-21-5, (R)-(+)-3-Pyrrolidinol 2969-81-5, Ethyl 4-bromobutyrate 3173-56-6, Benzyl isocyanate 3282-30-2, 2,2-Dimethylpropanoyl chloride 3529-08-6, 1-Piperidinepropanamine 3586-14-9, 3-Phenoxytoluene 3964-56-5, 4-Bromo-2-chlorophenol 4097-89-6 4318-37-0, N-Methylhomopiperazine 4524-93-0, Cyclopentanecarbonyl chloride 4530-20-5, N-(tert-Butoxycarbonyl)glycine 4727-72-4, 1-Benzyl-4-hydroxypiperidine 4746-97-8, 1,4-Dioxaspiro[4.5]decan-8-one 4892-89-1, 1-(2-Morpholinoethyl)piperazine 5036-48-6, N-(3-Aminopropyl)imidazole 5382-16-1, 4-Hydroxypiperidine 5464-28-8, 1,3-Dioxolane-4-methanol 6168-72-5 6602-54-6, 2-Chloronicotinonitrile 6850-38-0, 2-Aminocyclohexanol 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 7368-78-7, 4-Bromoguaiacol 7462-74-0, 2-Bromo-2-methylpropanamide 7663-77-6, 1-(3-Aminopropyl)-2-pyrrolidinone 10111-08-7, 1H-Imidazole-2-carboxaldehyde 10221-56-4 10316-79-7, 1-Amino-1-cyclopentanemethanol 13552-21-1, 1-Amino-2-butanol 13694-84-3 16369-05-4, 2-Amino-3-methyl-1-butanol 17082-09-6, (E)-Cinnamoyl chloride 17342-08-4 17702-83-9, N-(8-Bromooctyl)phthalimide 18853-55-9 19764-58-0, N2,N2-Dimethyl-1,2-propanediamine 20173-24-4, 3-(2-Aminoethyl)pyridine 20412-38-8, Neopentyl chloroformate 22795-97-7 23159-07-1, 1-Pyrrolidinepropanamine 23356-96-9, (S)-(+)-2-Pyrrolidinemethanol 23511-05-9 24304-84-5, 2-((2-Aminoethyl)thio)ethanol 26116-12-1, 2-(Aminomethyl)-1-ethylpyrrolidine 26177-44-6, 4-Bromobenzylamine hydrochloride 26394-17-2, Cyclopentanesulfonyl chloride 27578-60-5, 1-(2-Aminoethyl)piperidine 28179-33-1, 2-Bromo-4'-phenoxyacetophenone 34610-36-1 35166-33-7, (5-Methyl-3-isoxazolyl)methanol 39890-46-5 39901-94-5, 2-Pyridinecarbonyl chloride hydrochloride 40499-83-0, Pyrrolidin-3-ol 50893-53-3, α-Chloroethyl chloroformate 51067-38-0, 4-Phenoxyphenylboronic acid 53369-71-4, N,N-Dimethylneopentanediamine 55458-67-8, 1,3-Dimethyl-5-pyrazolecarbonyl chloride 56344-32-2, N-(3-Hydroxypropyl)ethylenediamine 61278-21-5, 1,2-Propanediol, 3-amino-, (S)- 64248-64-2, 2,5-Difluorobenzonitrile 66211-46-9 79099-07-3, N-tert-Butoxycarbonyl-4-piperidone 82417-45-6, 2,3-Dichlorobenzenesulfonyl chloride 86087-23-2, (S)-3-Hydroxytetrahydrofuran 93777-26-5, 5-Bromo-2-fluorobenzaldehyde 97986-34-0 105942-08-3, 4-Bromo-2-fluorobenzonitrile 113451-59-5 116183-82-5, (3R)-(+)-3-Aminopyrrolidine 123148-78-7 132958-72-6, (3R)-(+)-3-(Dimethylamino)pyrrolidine 137049-00-4, 1-Methylimidazole-4-sulfonyl chloride 146631-00-7, 4-(Benzyloxy)phenylboronic acid 195046-28-7 213743-76-1 213744-35-5 262433-02-3 262433-41-0 262433-42-1 262433-49-8 262442-03-5 262442-79-5 262444-52-0 262444-53-1 262444-54-2 **262444-55-3** 262444-56-4 262444-57-5 262444-58-6 262444-59-7 262444-60-0 262444-61-1 262444-62-2 262444-63-3 262444-65-5 330794-10-0 364354-29-0, 7-(1-Oxaspiro[2.5]oct-6-yl)-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine 364354-33-6 364354-35-8 364355-50-0 364355-52-2
RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 262431-69-6P 262433-52-3P 262439-86-1P 262439-87-2P 262439-88-3P
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262440-11-9P **262440-12-0P** 262440-13-1P 262440-14-2P
262440-15-3P 262440-16-4P 262440-17-5P **262440-18-6P**
262440-19-7P 262440-20-0P 262440-21-1P 262440-22-2P 262440-23-3P
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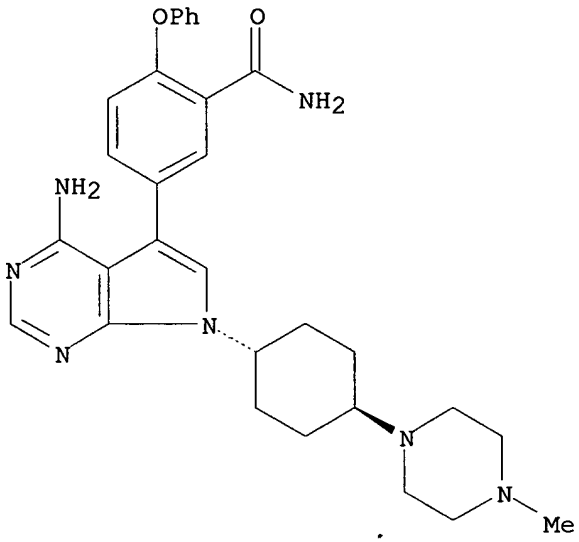
262442-49-9P 262442-51-3P 262442-53-5P 262442-55-7P 262442-57-9P
262442-59-1P 262442-60-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

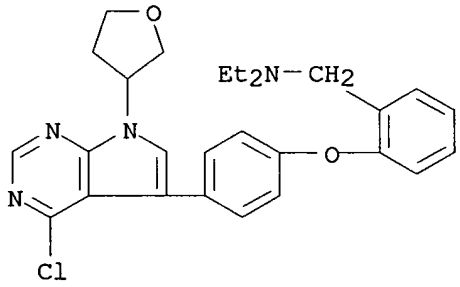
IT **364353-94-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolopyrimidinamines as protein kinase inhibitors)
RN 364353-94-6 HCAPLUS
CN Benzamide, 5-[4-amino-7-[trans-4-(4-methyl-1-piperazinyl)cyclohexyl]-7H-pyrrolo[2,3-d]pyrimidin-5-yl]-2-phenoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.

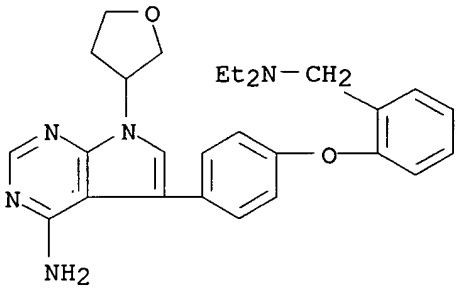


IT **262444-55-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)
RN 262444-55-3 HCAPLUS
CN Benzenemethanamine, 2-[4-[4-chloro-7-(tetrahydro-3-furanyl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl]phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)

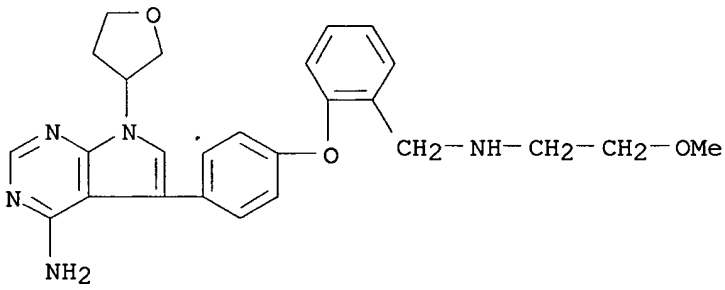


IT **262440-12-0P 262440-18-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

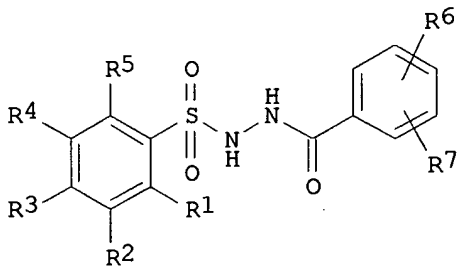
RN 262440-12-0 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[(diethylamino)methyl]phenoxy]phenyl]-7-(tetrahydro-3-furanyl)- (9CI) (CA INDEX NAME)



RN 262440-18-6 HCAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 5-[4-[2-[[(2-methoxyethyl)amino]methyl]phenoxy]phenyl]-7-(tetrahydro-3-furanyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



I

AB The title compds. [I; R3 = H, halo, alkyl, CO2H, (un)substituted alkoxy; R1, R2, R4, R5 = H, alkyl, halo, NO2, OCF3, CF3; R6, R7 = H, halo, alkyl, etc.] which are BCAT inhibitors and therefore are useful for treating or

preventing neuronal loss associated with stroke, ischemia, CNS trauma, hypoglycemia and surgery, as well as treating neurodegenerative diseases including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease and Down's syndrome, treating or preventing the adverse consequences of the overstimulation of the excitatory amino acids, treating anxiety, psychosis, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headache, chronic pain, **neuropathic** pain, Parkinson's disease, diabetic retinopathy, glaucoma, CMV retinitis, urinary incontinence, opioid tolerance or withdrawal, and inducing anesthesia, as well as for enhancing cognition, were prepared Thus, treating 4-nitrobenzoic acid with N-methylmorpholine and iso-Bu chloroformate in THF followed by addition of benzenesulfonyl hydrazide afforded 65% I [R1-R5 = H; R6 = 4-NO2; R7 = H] which showed IC50 of 40 μM in in vitro human branched chain amino acid-dependent aminotransferase cytosolic form (hBCATc) assay. Pharmaceutical composition containing compound I is claimed.

2003:414214 Document Number 139:6681 Preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases. Hu, Lain-yen; Kesten, Suzanne Ross; Lei, Huangshu; Wustrow, David Juergen; Ryder, Todd Robert (Warner-Lambert Company, USA). Eur. Pat. Appl. EP 1314723 A1 20030528, 37 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK. (English). CODEN: EPXXDW. APPLICATION: EP 2002-258017 20021121. PRIORITY: US 2001-PV333636 20011127.

AB . . . of the overstimulation of the excitatory amino acids, treating anxiety, psychosis, convulsions, aminoglycoside antibiotics-induced hearing loss, migraine headache, chronic pain, **neuropathic** pain, Parkinson's disease, diabetic retinopathy, glaucoma, CMV retinitis, urinary incontinence, opioid tolerance or withdrawal, and inducing anesthesia, as well as. . .

IT Analgesics
(treatment of or prevention of chronic pain and **neuropathic** pain; preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors)

IT 38064-61-8P 38064-68-5P 337470-74-3P 443638-38-8P 533881-82-2P
533881-83-3P 533881-84-4P 533881-85-5P 533881-86-6P 533881-87-7P
533881-88-8P 533881-89-9P 533881-90-2P 533881-91-3P 533881-92-4P
533881-93-5P 533881-94-6P 533881-95-7P 533881-96-8P 533881-97-9P
533881-98-0P 533881-99-1P 533882-00-7P **533882-01-8P**
533882-02-9P 533882-03-0P 533882-04-1P 533882-05-2P 533882-07-4P
533882-08-5P 533882-10-9P 533882-12-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases)

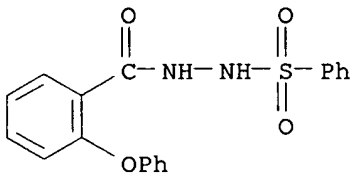
IT 62-23-7, 4-Nitro benzoic acid 80-17-1, Benzenesulfonyl hydrazide 98-09-9, Benzenesulfonyl chloride 98-59-9, (4-Methylphenyl)sulfonyl chloride 98-68-0, (4-Methoxybenzene)sulfonyl chloride 98-73-7, 4-tert-Butyl benzoic acid 100-52-7, Benzaldehyde, reactions 349-88-2, (4-Fluorobenzene)sulfonyl chloride 536-74-3, Phenylacetylene 616-83-1, (4-Methyl-3-nitro)benzenesulfonyl chloride 619-58-9, 4-Iodobenzoic acid 776-04-5, 2-Trifluoromethylbenzenesulfonyl chloride 917-92-0, 3,3-Dimethylbutyne 1486-51-7, 4-Benzyloxybenzoic acid 1623-92-3,

[(4-Phenoxy)benzene]sulfonyl chloride 1899-93-0, (3-Methylbenzene)sulfonyl chloride 2215-77-2, 4-Phenoxybenzoic acid 2243-42-7, 2-Phenoxybenzoic acid 2905-23-9, 2-(Chlorophenyl)sulfonyl chloride 2905-24-0, 3-(Bromophenyl)sulfonyl chloride 2991-42-6, 4-[(Trifluoromethyl)phenyl]sulfonyl chloride 3739-38-6, 3-Phenoxybenzoic acid 4187-88-6, 3-Cyclohexyl-3-hydroxy-1-propyne 16712-69-9, (4-Ethylbenzene)sulfonyl chloride 17715-00-3, 3-Cyclohexyl-1-propyne 18622-23-6, Biphenyl-4-carboxylic acid hydrazide 23095-31-0, (3,4-Dimethoxyphenyl)sulfonyl chloride 25300-37-2, (2-Chloro-6-methylbenzene)sulfonyl chloride **43038-37-5**, 2-Phenoxybenzoic acid hydrazide 51527-73-2, (2,4,6-Trichlorophenyl)sulfonyl chloride 54997-92-1, (4-n-Butylbenzene)sulfonyl chloride 73948-18-2, (4-n-Pentylbenzene)sulfonyl chloride 103008-51-1, 2-(Trifluoromethoxy)benzenesulfonyl chloride 146949-07-7, (4-n-Propylbenzene)sulfonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases)

IT **533882-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases)

RN 533882-01-8 HCAPLUS

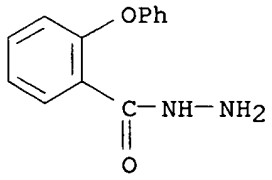
CN Benzoic acid, 2-phenoxy-, 2-(phenylsulfonyl)hydrazide (9CI) (CA INDEX NAME)



IT **43038-37-5**, 2-Phenoxybenzoic acid hydrazide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzoic acid 2-(phenylsulfonyl) hydrazides as branched chain amino acid-dependent aminotransferase inhibitors and their use in the treatment of neurodegenerative diseases)

RN 43038-37-5 HCAPLUS

CN Benzoic acid, 2-phenoxy-, hydrazide (9CI) (CA INDEX NAME)



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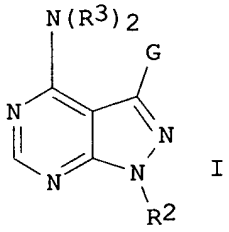

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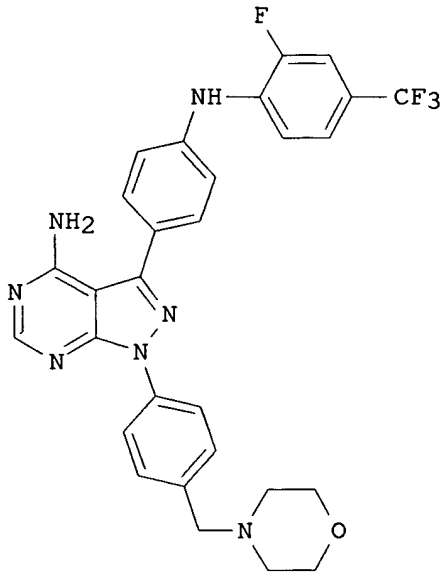

II

AB Title compds. I [wherein G = (un)substituted 5-6 membered (azahetero)aryl; R2 = H or (un)substituted trityl, cycloalkenyl, azaheteroaryl, or C6H4-4-CH2E; E = (un)substituted alkyl-OR, alkyl-CO2R, alkylheteroaryl, alkylheterocycloalkyl, or alkyl-NR2; R = independently H or (un)substituted (cyclo)alkyl, or aryl(alkyl); R3 = independently H, OH, or (un)substituted alkyl, alkyl-CO, (hetero)aryl-CO, or alkoxy; or racemic diastereomeric mixts., optical isomers, pharmaceutically acceptable salts, prodrugs, and/or biol. active metabolites thereof] were prepared For example, 3-iodo-1H-pyrazolo[3,4-d]pyrimidin-4-amine was coupled with 4-fluorobenzaldehyde in the presence of NaH in DMF to give 4-(4-amino-3-iodo-1H-pyrazolo[3,4-d]pyrimidin-1-yl)benzaldehyde. Treatment of the 3-iodopyrazolopyrimidine with N-[2-methoxy-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-2-fluoro-4-(trifluoromethyl)benzamide, Pd(PPh3)4, and Na2CO3 in H2O afforded the N-[4-(pyrazolopyrimidin-3-yl)phenyl]benzamide. Addition of morpholine to the benzaldehyde in the presence of Na(AcO)3BH in dichloroethane produced II. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at concentration of ≤ 50 μM. Certain compds. of the invention also significantly inhibited cdc2 or cellular VEGF-induced KDR tyrosine kinase phosphorylation at concns. of ≤ 50 μM. Thus, I are useful for the treatment of a wide variety of disease states ameliorated by the inhibition of protein tyrosine kinase activity essential for angiogenic processes (no data).

2002:793426 Document Number 137:310925 Preparation of 3-(azahetero)aryl-1H-pyrazolo[3,4-d]pyrimidin-3-amines as protein kinase inhibitors with antiangiogenic properties. Hirst, Gavin C.; Rafferty, Paul; Ritter, Kurt; Calderwood, David; Wishart, Neil; Arnold, Lee D.; Friedman, Michael M. (Abbott G.m.b.H. & Co. K.-G., Germany). PCT Int. Appl. WO 2002080926 A1

Delacroix

20021017, 867 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9104 20020322. PRIORITY: US 2001-815310 20010322.

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FILE 'EMBASE' ENTERED AT 19:09:24 ON 11 JAN 2005

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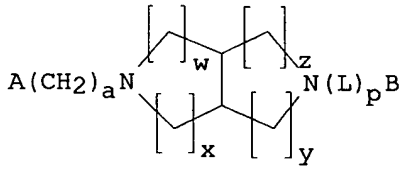

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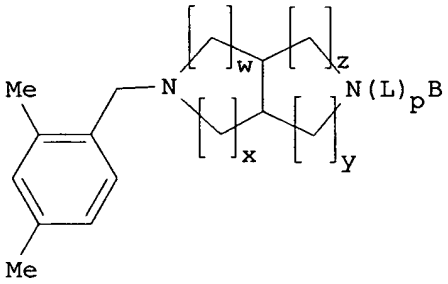

II

AB Chemokine receptor antagonists, in particular, bicyclic diamines (shown as I; e.g. N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide) that act as antagonists of chemokine CCR2 and CCR3 receptors including pharmaceutical compns. and uses thereof to treat or prevent diseases associated with monocyte accumulation, lymphocyte accumulation or leukocyte accumulation are described herein. In I, A is a substituted or unsubstituted (C1-C6)alkyl, substituted or unsubstituted (C2-C6)alkenyl, substituted or unsubstituted partially saturated or fully saturated (C3-C6)cycloalkyl, substituted or unsubstituted partially saturated or fully saturated 5 to 6 membered heterocyclic ring, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl group. A is 0-3; w, x, y and z are each independently 0-4 with provisos; p is 0 or 1. L is a linking group selected from -(CH2)q-X-, where X is NH, O, or oxo and q is 0-4, -S(O)r-(CH2)t-NH-, where r is 0-2 and t is 0-4,

-(aryl)-NH-, -(heteroaryl)-NH-, and an amino acid residue where the amino N of said amino acid residue is attached to B and the carbonyl of said amino acid residue is attached to the ring N. B is a substituted or unsubstituted (C1-C6)alkylcarbonyl, arylcarbonyl, (C1-C6)alkoxycarbonyl, aryloxycarbonyl, (C1-C6)alkylsulfonyl, arylsulfonyl, (C1-C6)alkylthiocarbonyl, arylthiocarbonyl, (C1-C6)alkylcarbamoyl, arylcarbamoyl, (C1-C6)alkyl-C(:NH)-, substituted or unsubstituted aryl-C(:NH)-, or a protecting group;. Although the methods of preparation are not claimed, several example prepns. are included and about 1500 specific compds. are listed with their HPLC retention times and CI-MS mol. wts. In general, the compds. listed in the Examples provided CCR2 activity based on chemotaxis from .apprx.5 to .apprx.100% inhibition at 1 μM concentration Compds. II (R = Me) provided higher activity for inhibition of binding to its CCR2 receptor and showed less activity for inhibition of binding to the CCR3 receptor. Whereas, compds. II (R = Cl) provided higher activity for inhibition of binding to the CCR3 receptor and less activity for binding to the CCR2 receptor.

2002:695987 Document Number 137:232638 Preparation of bicyclic diamines as CCR2 and CCR3 chemokine receptor antagonists for treating/preventing diseased associated with monocyte, lymphocyte or leukocyte accumulation. Colon-Cruz, Roberto; Didiuk, Mary Theresa; Duffy, Erin Maureen; Garigipati, Ravi Shanker; Lau, Wan Fang; McDonald, Wayne Scott (Pfizer Products Inc., USA). PCT Int. Appl. WO 2002070523 A1 20020912, 165 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB238 20020124. PRIORITY: US 2001-PV273984 20010307.

IT Antirheumatic agents
Atherosclerosis
Eczema
Encephalomyelitis
Human
Psoriasis
Rheumatoid arthritis
Transplant rejection
Wound healing
Wound healing promoters
(preparation of bicyclic diamines as CCR2 and CCR3 chemokine receptor antagonists for treating/preventing diseased associated with monocyte, lymphocyte or leukocyte accumulation)

IT 455909-13-4P, N-[2-Oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-trifluoromethoxybenzamide 455909-14-5P, N-[2-Oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-trifluoromethoxybenzamide 455909-15-6P, 3,4,5-Trifluoro-N-[2-oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-16-7P, 3,4,5-Trifluoro-N-[2-oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-17-8P, N-[2-Oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-propylbenzamide 455909-18-9P, N-[2-Oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-propylbenzamide 455909-19-0P, N-[2-[5-(2-Fluoro-4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-

propylbenzamide 455909-20-3P, N-[2-[5-(4-Fluoro-2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-propylbenzamide 455909-21-4P, 4-Isopropoxy-N-[2-oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-22-5P, 4-Isopropoxy-N-[2-oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-23-6P, N-[2-[5-(2-Fluoro-4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-isopropoxybenzamide 455909-24-7P, N-[2-[5-(4-Fluoro-2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-isopropoxybenzamide 455909-25-8P, N-[2-Oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-propoxybenzamide 455909-26-9P, N-[2-Oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-4-propoxybenzamide 455909-27-0P, N-[2-[5-(2-Fluoro-4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-propoxybenzamide 455909-28-1P, N-[2-[5-(4-Fluoro-2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-propoxybenzamide 455909-29-2P, 3-Chloro-4-fluoro-N-[2-oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-30-5P, 3-Chloro-4-fluoro-N-[2-oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-31-6P, 3-Chloro-4-fluoro-N-[2-[5-(4-fluoro-2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-32-7P, 3-Fluoro-N-[2-oxo-2-[5-(4-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-5-trifluoromethylbenzamide 455909-33-8P, 3-Fluoro-N-[2-oxo-2-[5-(2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-5-trifluoromethylbenzamide 455909-34-9P, 3-Fluoro-N-[2-[5-(4-fluoro-2-trifluoromethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-5-trifluoromethylbenzamide 455909-35-0P, N-[2-[5-((1-Methyl-1H-indol-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-36-1P, 4-Chloro-N-[2-[5-((1-Methyl-1H-indol-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-37-2P, 3,4-Dichloro-N-[2-[5-((1-Methyl-1H-indol-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-38-3P, 3-Chloro-N-[2-[5-((1-Methyl-1H-indol-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-39-4P, N-[2-Oxo-2-[5-[(quinolin-3-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-3-trifluoromethylbenzamide 455909-40-7P, 3,4-Dichloro-N-[2-oxo-2-[5-((quinolin-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-41-8P, 3-Chloro-N-[2-oxo-2-[5-((quinolin-3-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-42-9P, 4-Chloro-N-[2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-43-0P, N-[2-[5-(4-Chlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-44-1P, 4-Chloro-N-[2-[5-(4-chlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-45-2P, 3,4-Dichloro-N-[2-[5-(4-chlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-46-3P, 3-Chloro-N-[2-[5-(4-chlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-47-4P, N-[2-[5-(5-Bromo-2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-48-5P, N-[2-[5-(5-Bromo-2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455909-49-6P, N-[2-[5-(5-Bromo-2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,4-dichlorobenzamide 455909-50-9P, N-[2-[5-(5-Bromo-2-

methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-chlorobenzamide 455909-51-0P, N-[2-[5-(3-Bromo-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-52-1P, N-[2-[5-(3-Bromo-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455909-53-2P, N-[2-[5-(3-Bromo-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-chlorobenzamide 455909-54-3P, N-[2-[5-(3,5-Dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-55-4P, 4-Chloro-N-[2-[5-(3,5-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-56-5P, 3,4-Dichloro-N-[2-[5-(3,5-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-57-6P, 3-Chloro-N-[2-[5-(3,5-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-58-7P, N-[2-[5-(3-Bromo-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-59-8P, N-[2-[5-(3-Bromo-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455909-60-1P, N-[2-[5-(3-Bromo-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,4-dichlorobenzamide 455909-61-2P, N-[2-[5-(3-Bromo-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-chlorobenzamide 455909-62-3P, N-[2-[5-(3-Chloro-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-63-4P, 4-Chloro-N-[2-[5-(3-chloro-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-64-5P, 3,4-Dichloro-N-[2-[5-(3-chloro-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-65-6P, 3-Chloro-N-[2-[5-(3-chloro-4-fluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-66-7P, N-[2-[5-(4-Bromobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-67-8P, N-[2-[5-(4-Bromobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455909-68-9P, N-[2-[5-(4-Bromobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,4-dichlorobenzamide 455909-69-0P, N-[2-[5-(4-Bromobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-chlorobenzamide 455909-70-3P, N-[2-[5-(3,4-Dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-71-4P, 4-Chloro-N-[2-[5-(3,4-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-72-5P, 3,4-Dichloro-N-[2-[5-(3,4-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-73-6P, 3-Chloro-N-[2-[5-(3,4-dichlorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-74-7P, 3-Chloro-N-[2-[5-(2-methylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-75-8P, 4-Chloro-N-[2-[5-(2-methylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-76-9P, N-[2-[5-(Biphenyl-4-ylmethyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455909-77-0P, N-[2-[5-(Biphenyl-4-ylmethyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,4-dichlorobenzamide 455909-78-1P, N-[2-[5-(Biphenyl-4-ylmethyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]2-oxoethyl]-3-chlorobenzamide 455909-79-2P, N-[2-Oxo-2-[5-(3-phenoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-3-trifluoromethylbenzamide 455909-80-5P, 4-Chloro-N-[2-oxo-2-[5-(3-phenoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-81-6P, 3,4-Dichloro-N-[2-oxo-2-[5-(3-phenoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-82-7P, 3-Chloro-N-[2-oxo-2-[5-(3-phenoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-83-8P, N-[2-[5-((2-

Methoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-84-9P, 4-Chloro-N-[2-[5-((2-methoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-85-0P, 3,4-Dichloro-N-[2-[5-((2-methoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-86-1P, 3-Chloro-N-[2-[5-((2-methoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-87-2P, N-[2-[5-((2-Ethoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-88-3P, 4-Chloro-N-[2-[5-((2-ethoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-89-4P, 3,4-Dichloro-N-[2-[5-((2-ethoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-90-7P, 3-Chloro-N-[2-[5-((2-ethoxynaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-91-8P, N-[2-Oxo-2-[5-(3-p-tolyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-3-trifluoromethylbenzamide 455909-92-9P, 4-Chloro-N-[2-oxo-2-[5-(3-p-tolyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-93-0P, 3,4-Dichloro-N-[2-oxo-2-[5-(3-p-tolyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-94-1P, 3-Chloro-N-[2-oxo-2-[5-(3-p-tolyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455909-95-2P, N-[2-[5-((4-Methylnaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455909-96-3P, 4-Chloro-N-[2-[5-((4-methylnaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-97-4P, 3,4-Dichloro-N-[2-[5-((4-methylnaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-98-5P, 3-Chloro-N-[2-[5-((4-methylnaphthalen-1-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455909-99-6P, N-[2-[5-((2'-Methylbiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-00-6P, 4-Chloro-N-[2-[5-((2'-methylbiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-01-7P, 3,4-Dichloro-N-[2-[5-((2'-methylbiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-02-8P, 3-Chloro-N-[2-[5-((2'-methylbiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-03-9P, N-[2-[5-((2'-Methoxybiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-04-0P, 4-Chloro-N-[2-[5-((2'-methoxybiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-05-1P, 3,4-Dichloro-N-[2-[5-((2'-methoxybiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-06-2P, 3-Chloro-N-[2-[5-((2'-methoxybiphenyl-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-07-3P, N-[2-[5-((6-Methoxynaphthalen-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-08-4P, 3,4-Dichloro-N-[2-[5-((6-methoxynaphthalen-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-09-5P, 3-Chloro-N-[2-[5-((6-methoxynaphthalen-2-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-10-8P, 4-Chloro-N-[2-[5-(2,4-dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-11-9P, 3-Chloro-N-[2-[5-(2,4-dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-13-1P, N-[2-[5-(2-Methylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-15-3P, 3,4-Dichloro-N-[2-[5-(2-methylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-17-5P, N-[2-[5-(2-Ethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-19-7P, 4-Chloro-N-[2-[5-(2-

ethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-21-1P, 3,4-Dichloro-N-[2-[5-(2-ethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-23-3P, 3-Chloro-N-[2-[5-(2-ethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-25-5P, N-[2-[5-(2-Methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-27-7P, 4-Chloro-N-[2-[5-(2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-29-9P, 3,4-Dichloro-N-[2-[5-(2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-31-3P, 3-Chloro-N-[2-[5-(2-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-33-5P, N-[2-[5-(2,5-Dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-34-6P, 4-Chloro-N-[2-[5-(2,5-dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-36-8P, 3,4-Dichloro-N-[2-[5-(2,5-dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-38-0P, 3-Chloro-N-[2-[5-(2,5-dimethoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-40-4P, N-[2-[5-(2,5-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-42-6P, 4-Chloro-N-[2-[5-(2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-44-8P, 3,4-Dichloro-N-[2-[5-(2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-46-0P, 3-Chloro-N-[2-[5-(2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-48-2P, N-[2-[5-(4-Methoxy-2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-50-6P, 4-Chloro-N-[2-[5-(4-methoxy-2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-52-8P, 3,4-Dichloro-N-[2-[5-(4-methoxy-2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-54-0P, 3-Chloro-N-[2-[5-(4-methoxy-2,5-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-56-2P, N-[2-[5-(4-Methoxy-2,3-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-58-4P, 4-Chloro-N-[2-[5-(4-methoxy-2,3-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-60-8P, 3,4-Dichloro-N-[2-[5-(4-methoxy-2,3-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-62-0P, 3-Chloro-N-[2-[5-(4-methoxy-2,3-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-64-2P, N-[2-[5-(2-Benzyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-66-4P, N-[2-[5-(2-Benzyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-chlorobenzamide 455910-67-5P, N-[2-[5-(2-Benzyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,4-dichlorobenzamide 455910-68-6P, N-[2-[5-(2-Benzyloxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-chlorobenzamide 455910-69-7P, N-[2-[5-(3-Cyclopentyloxy-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-70-0P, 4-Chloro-N-[2-[5-(3-cyclopentyloxy-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-71-1P, 3,4-Dichloro-N-[2-[5-(3-cyclopentyloxy-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-72-2P, 3-Chloro-N-[2-[5-(3-cyclopentyloxy-4-methoxybenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-73-3P, 3,4-Dichloro-N-[2-[hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-74-4P, 1H-Indole-2-carboxylic acid [2-oxo-2-[5-[(quinolin-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]amide 455910-75-5P, 2-Amino-5-chloro-N-[2-oxo-2-[5-[(quinolin-2-

yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-76-6P, 2-Amino-5-bromo-N-[2-oxo-2-[5-[(quinolin-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-77-7P, 3,4-Dichloro-N-[2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-78-8P, 1H-Indole-2-carboxylic acid [2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]amide 455910-79-9P, 3-Bromo-4-chloro-N-[2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-80-2P, 2-Amino-5-chloro-N-[2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-81-3P, 2-Amino-5-bromo-N-[2-oxo-2-[5-((quinolin-4-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]benzamide 455910-82-4P, N-[2-Oxo-2-[5-[(quinolin-4-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethyl]-3-trifluoromethylbenzamide 455910-83-5P, 1H-Indole-2-carboxylic acid [2-[5-[(naphthalen-1-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455910-84-6P, 2-Amino-5-chloro-N-[2-[5-[(naphthalen-1-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-85-7P, 2-Amino-5-bromo-N-[2-[5-[(naphthalen-1-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-86-8P, 2-Amino-5-chloro-N-[2-[5-[(naphthalen-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-87-9P, 2-Amino-5-bromo-N-[2-[5-[(naphthalen-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455910-88-0P, 2-Amino-1-[5-[(quinolin-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethanone 455910-89-1P, 2-Amino-1-[5-[(quinolin-4-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethanone 455910-90-4P, 2-Amino-1-[5-[(naphthalen-1-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethanone 455910-91-5P, 2-Amino-1-[5-[(naphthalen-2-yl)methyl]hexahydropyrrolo[3,4-c]pyrrol-2-yl]ethanone 455910-92-6P, N-[2-[5-(2,4-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,5-bis(trifluoromethyl)benzamide 455910-93-7P, N-[2-[5-(2,4-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-94-8P, N-[2-[5-(2,5-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3,5-bis(trifluoromethyl)benzamide 455910-95-9P, N-[2-[5-(2,5-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455910-96-0P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluoro-3-trifluoromethylbenzamide **455910-97-1P**, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-phenoxybenzamide 455910-98-2P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-5-fluoro-2-methylbenzamide 455910-99-3P, 3-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluorobenzamide 455911-00-9P, 2-Amino-5-bromo-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-01-0P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-methyl-5-nitrobenzamide 455911-02-1P, 2-Amino-5-chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-03-2P, 5-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-nitrobenzamide 455911-04-3P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-nitro-5-trifluoromethylbenzamide 455911-05-4P, 2-Amino-N-[2-[5-(2,4-difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-5-iodobenzamide 455911-06-5P, 2-Amino-N-[2-[5-(2,4-difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-

oxoethyl]-5-nitrobenzamide 455911-07-6P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-ethoxybenzamide 455911-08-7P, 2,4-Dichloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-09-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,6-difluorobenzamide 455911-10-1P, 2-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-6-fluorobenzamide 455911-11-2P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,4-difluorobenzamide 455911-12-3P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,3-difluorobenzamide 455911-13-4P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-trifluoromethylbenzamide 455911-14-5P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,3,4-trifluorobenzamide 455911-15-6P, 2,3-Dichloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-16-7P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,4-bis(trifluoromethyl)benzamide 455911-17-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluoro-4-trifluoromethylbenzamide 455911-18-9P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-fluoro-2-trifluoromethylbenzamide 455911-19-0P, 2-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4-fluorobenzamide 455911-20-3P, 2-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-4,5-difluorobenzamide 455911-21-4P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,4,5-trifluorobenzamide 455911-22-5P, 3-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,6-dimethoxybenzamide 455911-23-6P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluoro-6-trifluoromethylbenzamide 455911-24-7P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-trifluoromethoxybenzamide 455911-25-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,3,6-trimethoxybenzamide 455911-26-9P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,6-dimethoxybenzamide 455911-27-0P, 4-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluorobenzamide 455911-28-1P, 2-Amino-3,5-dibromo-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-29-2P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-fluoro-5-trifluoromethylbenzamide 455911-30-5P, 2-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455911-31-6P, 2-Acetylamino-5-bromo-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]benzamide 455911-32-7P, 2-Amino-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-trifluoromethylbenzamide 455911-33-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-methoxybenzamide 455911-34-9P, 2-Amino-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-5-fluorobenzamide 455911-35-0P, 2-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]isoindole-1,3-dione 455911-36-1P, Naphthalene-2-carboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-37-2P, N-[2-[5-(2,4-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-(2-

trifluoromethylphenyl)acetamide 455911-38-3P, N-[2-[5-(2,5-Difluorobenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-(2-trifluoromethylphenyl)acetamide 455911-39-4P, 5-Chloro-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-methylbenzamide 455911-40-7P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,5-bis(trifluoromethyl)benzamide 455911-41-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-nitrobenzamide 455911-42-9P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-methylbenzamide 455911-43-0P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2,5-dimethylbenzamide 455911-44-1P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-3-(4-hydroxyphenyl)propionamide 455911-45-2P, 1-(4-Methoxyphenyl)cyclopropanecarboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-46-3P, 1-(4-Chlorophenyl)cyclopropanecarboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-47-4P, 1-p-Tolylcyclopropanecarboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-48-5P, 2-(4-Chlorophenyl)-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]isobutyramide 455911-49-6P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-(2-fluorobiphenyl-4-yl)propionamide 455911-50-9P, 1H-Indole-3-carboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-51-0P, 1-(4-Chlorophenyl)-5-trifluoromethyl-1H-pyrazole-4-carboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-52-1P, 1-Phenyl-5-trifluoromethyl-1H-pyrazole-4-carboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-53-2P, 5-Methyl-1-phenyl-1H-pyrazole-4-carboxylic acid [2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]amide 455911-54-3P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-(2-trifluoromethylphenyl)acetamide 455911-55-4P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-(naphthalen-1-yl)acetamide 455911-56-5P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-phenylacetamide 455911-57-6P, 2-(Biphenyl-4-yl)-N-[2-[5-(2,4-dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]acetamide 455911-58-7P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-o-tolylacetamide 455911-59-8P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-m-tolylacetamide 455911-60-1P, N-[2-[5-(2,4-Dimethylbenzyl)hexahydropyrrolo[3,4-c]pyrrol-2-yl]-2-oxoethyl]-2-p-tolylacetamide 455911-61-2P,

---- PARAGRAPH TRUNCATED DUE TO SIZE LIMITATIONS ----

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicyclic diamines as CCR2 and CCR3 chemokine receptor antagonists for treating/preventing diseased associated with monocyte, lymphocyte or leukocyte accumulation)

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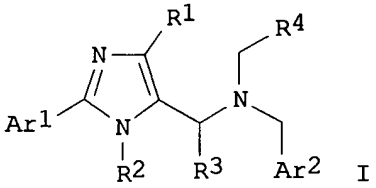
GI



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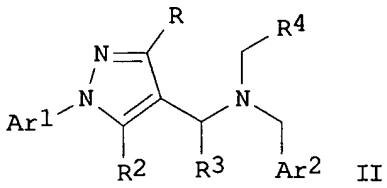

II

AB The invention includes low mol. weight, non-peptidic, non-peptidommetic, organic mols. that can act as modulators of mammalian complement C5a receptors, preferably ones that act as high affinity C5a receptor ligands and also such ligands that can act as antagonists or inverse agonists of complement C5a receptors. Preferred compds. of the invention possess some or all of the following properties in that they are: (1) multi-aryl in structure; (2) heteroaryl in structure; (3) a pharmaceutically acceptable oral dose can provide a detectable in vivo effect; (4) comprise fewer than four or preferably no amide bonds, and (5) capable of habiting leukocyte chemotaxis at nanomolar or sub-nanomolar concns. Such compds. include imidazoles I [R1 = H, OH, halo, etc.; R2 = alkyl, cycloalkyl, etc.; R3 H, alkyl, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.; Ar1, Ar2 = (un)substituted carbocyclic aryl, arylalkyl, etc.], pyrazoles II [R = H, OH, halo, etc.; R2, R3 = H, OH, halo, etc.; R4 = alkyl, alkenyl, cycloalkyl, etc.; Ar1, Ar2 = (un)substituted carbocyclic aryl, arylalkyl, etc.], amides Ar1CONR1R2 [III; R1, R2 = alkyl, alkenyl, cycloalkyl, etc.; Ar1 = (un)substituted carbocyclic aryl, arylalkyl, etc.], etc. Detailed preparation of some compds. I-III was given. E.g., a multi-step synthesis of I [Ar1 = Ph; R1, R3 = H; R2 = Bu; R4, Ar2 = 3,4-methylenedioxyphenyl] was presented. The invention also includes pharmaceutical composition comprising such compds. I-III and the use of such compds. in treating a variety of inflammatory and immune system disorders.

2002:487497 Document Number 137:78952 Preparation of substituted imidazoles, pyrazoles and amides as high affinity C5a receptor modulators. Thurkauf, Andrew; Zhang, Xiaoyan; He, Xia-Shu; Zhao, He; Peterson, John; Maynard, George; Ohliger, Robert (Neurogen Corporation, USA). PCT Int. Appl. WO 2002049993 A2 20020627, 609 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US26816 20000929.

IT Alzheimer's disease
Arteriosclerosis
Asthma
Autoimmune disease
Dermatomyositis
Multiple organ failure
Multiple sclerosis
Myasthenia gravis
Psoriasis
Rheumatoid arthritis
Sepsis

Transplant rejection
(treatment of; preparation of substituted imidazoles, pyrazoles and amides as high affinity C5a receptor modulators)

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439559-81-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted imidazoles, pyrazoles and amides as high affinity C5a receptor modulators)

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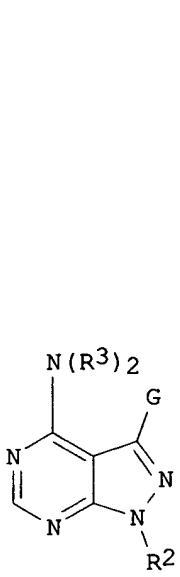
439569-26-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted imidazoles, pyrazoles and amides as high affinity C5a receptor modulators)

L5 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



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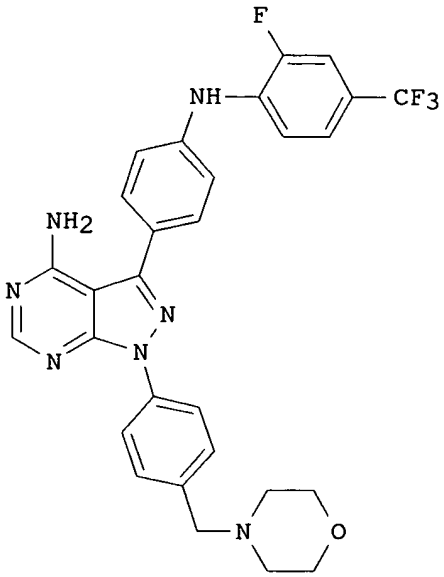

II

AB Title compds. I [wherein G = (un)substituted 5-6 membered (azahetero)aryl; R2 = H or (un)substituted trityl, cycloalkenyl, azaheteroaryl, or C6H4-4-CH2E; E = (un)substituted alkyl-OR, alkyl-CO2R, alkylheteroaryl, alkylheterocycloalkyl, or alkyl-NR2; R = independently H or (un)substituted (cyclo)alkyl, or aryl(alkyl); R3 = independently H, OH, or (un)substituted alkyl, alkyl-CO, (het'ero)aryl-CO, or alkoxy; or racemic diastereomeric mixts., optical isomers, pharmaceutically acceptable salts, prodrugs, and/or biol. active metabolites thereof] were prepared For example, 3-iodo-1H-pyrazolo[3,4-d]pyrimidin-4-amine was coupled with 4-fluorobenzaldehyde in the presence of NaH in DMF to give 4-(4-amino-3-iodo-1H-pyrazolo[3,4-d]pyrimidin-1-yl)benzaldehyde. Treatment of the 3-iodopyrazolopyrimidine with N-[2-methoxy-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-2-fluoro-4-(trifluoromethyl)benzamide, Pd(PPh3)4, and Na2CO3 in H2O afforded the N-[4-(pyrazolopyrimidin-3-yl)phenyl]benzamide. Addition of morpholine to the benzaldehyde in the presence of Na(AcO)3BH in dichloroethane produced II. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at concentration of ≤ 50 μM. Certain compds. of the invention also significantly inhibited cdc2 or cellular VEGF-induced KDR tyrosine kinase phosphorylation at concns. of ≤ 50 μM. Thus, I are useful for the treatment of a wide variety of disease states ameliorated by the inhibition of protein tyrosine kinase activity essential for angiogenic processes (no data).

2002:814851 Document Number 137:310930 Preparation of 3-(azahetero)aryl-1H-pyrazolo[3,4-d]pyrimidin-3-amines as protein kinase inhibitors with antiangiogenic properties. Hirst, Gavin C.; Rafferty, Paul; Ritter, Kurt; Calderwood, David; Wishart, Neil; Arnold, Lee D.; Friedman, Michael M. (Abbott Laboratories, USA). U.S. Pat. Appl. Publ. US 2002156081 A1 20021024, 426 pp., Cont.-in-part of U.S. Ser. Number 663,780. (English). CODEN: USXXCO. APPLICATION: US 2001-815310 20010322. PRIORITY: US 1999-PV154620 19990917; US 2000-663780 20000915.

330789-64-5P 330789-66-7P, Trans-3-[4-[(2-Furylmethyl)amino]phenyl]-1-[4-(4-methylpiperazino)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine diacetate 330789-68-9P, 3-[4-[[(5-Methyl-2-furyl)methyl]amino]phenyl]-1-

[1-(1-methyl-4-piperidyl)-4-piperidyl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine acetate 330789-70-3P 330789-71-4P 330789-77-0P 330789-79-2P 330789-81-6P 330789-83-8P 330789-85-0P 330789-86-1P 330789-88-3P 330789-90-7P 330789-92-9P 330789-93-0P 330789-96-3P 330789-98-5P, Cis-N-[4-[4-Amino-1-[4-(4-methylpiperazino)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]phenyl]-2-methyl-2-phenylpropanamide diacetate 330790-00-6P 330790-02-8P 330790-03-9P 330790-05-1P, Cis-N-[4-[4-Amino-1-[4-(4-methylpiperazino)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]phenyl]-1,3-benzoxazol-2-amine diacetate 330790-06-2P, 2-[4-(4-Amino-1-cyclopentyl-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenoxy]acetamide 330790-08-4P, 5-[4-(4-Amino-1-cyclopentyl-1H-pyrazolo[3,4-d]pyrimidin-3-yl)phenoxy]-2-furoic acid 330790-09-5P, 1-Cyclopentyl-3-[4-(3-thienyloxy)phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine 330790-11-9P 330790-12-0P, Cis-3-[3-[Di(2-furylmethyl)amino]phenyl]-1-[4-(4-methylpiperazino)cyclohexyl]-1H-pyrazolo[3,4-d]pyrimidin-4-amine **330790-14-2P** 330790-18-6P, (2S)-3-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]propane-1,2-diol 330790-19-7P, (2R)-3-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]propane-1,2-diol 330790-22-2P 330790-23-3P, N-Methyl-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-24-4P, N,N-Dimethyl-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-25-5P, N-Isopropyl-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-26-6P, N-(3-Hydroxypropyl)-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-27-7P 330790-28-8P, N-Benzyl-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-30-2P, 2-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-1-morpholino-1-ethanone 330790-31-3P, N-(3-Methyl-5-isoxazolyl)-2-[3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]acetamide 330790-34-6P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(2-hydroxyethyl)amino]-1-ethanone 330790-35-7P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(2-methoxyethyl)amino]-1-ethanone 330790-36-8P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(3-hydroxypropyl)amino]-1-ethanone 330790-37-9P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(2,3-dihydroxypropyl)amino]-1-ethanone 330790-38-0P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(tetrahydro-2-furanylmethyl)amino]-1-ethanone 330790-39-1P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(2-piperidinoethyl)amino]-1-ethanone 330790-40-4P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[[2-(dimethylamino)ethyl](methyl)amino]-1-ethanone 330790-42-6P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[[2-(dimethylamino)ethyl]amino]-1-ethanone acetate 330790-43-7P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[methyl(1-methyl-4-piperidyl)amino]-1-ethanone 330790-44-8P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(2-morpholinoethyl)amino]-1-ethanone 330790-45-9P, 1-[3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-azetanyl]-2-[(3-morpholinopropyl)amino]-1-ethanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of [(hetero)aryl]pyrazolo[3,4-d]pyrimidinamines as protein kinase inhibitors with a

SYSTEM LIMITS
EXCEEDED

L5 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The invention relates to a combination useful in treating **Multiple Sclerosis**, other **demyelinating** disorders and peripheral **neuropathy** in a mammal comprising a neurotransmitter-inducing or precursor agent in combination with an (serotonin reuptake inhibitors, SRI) anxiolytic agent or an antidepressant with improvement in efficiency. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a neurotransmitter-inducing or precursor agent, and an SRI antidepressant or anxiolytic agent.
2002:773622 Document Number 137:273225 Combination treatment for **multiple sclerosis**, other **demyelinating** conditions and peripheral **neuropathy**, especially painful **neuropathies** and diabetic **neuropathy**. Howard, Harry Ralph, Jr. (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1247533 A2 20021009, 15 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2002-251844 20020314. PRIORITY: US 2001-PV281988 20010405.
TI Combination treatment for **multiple sclerosis**, other **demyelinating** conditions and peripheral **neuropathy**, especially painful **neuropathies** and diabetic **neuropathy**
AB The invention relates to a combination useful in treating **Multiple Sclerosis**, other **demyelinating** disorders and peripheral **neuropathy** in a mammal comprising a neurotransmitter-inducing or precursor agent in combination with an (serotonin reuptake inhibitors, SRI) anxiolytic agent or. . .
ST **multiple sclerosis demyelinating** disease **neuropathy** combination therapy
IT Antidepressants
Anxiolytics
Drug delivery systems
Encephalomyelitis
Mammalia
Multiple sclerosis
Neurotransmitter agonists
(combination treatment for **multiple sclerosis**, **demyelinating** conditions and peripheral **neuropathy**)
IT Nerve, disease
(**demyelination**; combination treatment for **multiple sclerosis**, **demyelinating** conditions and peripheral **neuropathy**)
IT Nerve, disease
(diabetic **neuropathy**; combination treatment for **multiple sclerosis**, **demyelinating** conditions and peripheral **neuropathy**)
IT Nerve, disease
(**neuropathy**; combination treatment for **multiple sclerosis**, **demyelinating** conditions and peripheral **neuropathy**)
IT Nerve, disease
(peripheral **neuropathy**; combination treatment for

multiple sclerosis, demyelinating conditions and peripheral **neuropathy**)

IT **Multiple sclerosis**
(therapeutic agents; combination treatment for **multiple sclerosis, demyelinating** conditions and peripheral **neuropathy**)

IT 51-67-2, Tyramine 59-92-7, biological studies 60-18-4, L-Tyrosine, biological studies 63-91-2, L-Phenylalanine, biological studies 73-22-3, L-Tryptophan, biological studies **107624-14-6** **107624-14-6D**, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment for **multiple sclerosis, demyelinating** conditions and peripheral **neuropathy**)

IT 50-67-9, 5-HT, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reuptake inhibitors; combination treatment for **multiple sclerosis, demyelinating** conditions and peripheral **neuropathy**)

L5 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Chemical compds. having structural formula I and physiol. acceptable salts and metabolites thereof, are inhibitors of serine/threonine and tyrosine kinase activity. Several of the kinases, whose activity is inhibited by these chemical compds., are involved in immunol., hyperproliferative, or angiogenic processes. Thus, these chemical compds. can ameliorate disease states where angiogenesis or endothelial cell hyperproliferation is a factor. These compds. can be used to treat cancer and hyperproliferative disorders, rheumatoid arthritis, disorders of the immune system, transplant rejections and inflammatory disorders. All exemplified compds. significantly inhibited either FGFR, PDGFR, KDR, Tie-2, Lck, Fyn, Blk, Lyn, or Src at ≤50 μM, and some significantly inhibited cdc2 at ≤50 μM. In I, ring A is a six membered aromatic ring or a five or six membered heteroarom. ring which is optionally substituted. L is -O-, -S-, -S(O)-, -S(O)2-, -N(R)-, -N[C(O)OR]-, -N[C(O)R]-, -N(SO2R)-, -CH2O-; -CH2S-, -CH2N(R)-, -C(NR)-;-CH2N[C(O)R]-, -CH2N[C(O)OR]-, -CH2N(SO2R)-, -CH(NHR)-, -CH[NHC(O)R]-, -CH(NHSO2R)-, -CH[NHC(O)OR]-, -CH[OC(O)R]-, -CH[OC(O)NHR]-, -CH:CH-; -C(:NOR)-, -C(O)-, -CH(OR)-, -C(O)N(R)-, -N(R)C(O)-, -N(R)S(O)-, -N(R)S(O)2-, -OC(O)N(R)-, -N(R)C(O)N(R)-, -NRC(O)O-, -S(O)N(R)-, -S(O)2N(R)-, -N[C(O)R]S(O)-, -N[C(O)R]S(O)2-, -N(R)S(O)N(R)-, -N(R)S(O)2N(R)-, -C(O)N(R)C(O)-, -S(O)N(R)C(O)-, -S(O)2N(R)C(O)-, -OS(O)N(R)-, -OS(O)2N(R)-, -N(R)S(O)O-, -N(R)S(O)2O-, -N(R)S(O)C(O)-, -N(R)S(O)2C(O)-, -SON[C(O)R]-, -SO2N[C(O)R]-, -N(R)SON(R)-, -N(R)SO2N(R)-, -C(O)O-, -N(R)P(OR')O-, -N(R)P(OR')-, -N(R)P(O)(OR')O-, -N(R)P(O)(OR')-, -N[C(O)R]P(OR')O-, -N[C(O)R]P(OR')-, -N[C(O)R]P(O)(OR')O-, -N[C(O)R]P(OR')-, -CH(R)S(O)-, or -CH(R)S(O)2-. L is also -CH(R)N[C(O)OR]-, -CH(R)N[C(O)R]-, -CH(R)N(SO2R), -CH(R)O-, -CH(R)S-, -CH(R)N(R)-, -CH(R)N[C(O)R]-, - CH(R)N[C(O)OR]-, -CH(R)N(SO2R)-, -CH(R)C(:NOR)-, -CH(R)C(O)-, -CH(R)CH(OR)-, -CH(R)C(O)N(R)-, -CH(R)N(R)C(O)-, -CH(R)N(R)S(O)-, -CH(R)N(R)S(O)2-, -CH(R)OC(O)N(R)-,

-CH(R)N(R)C(O)N(R)-, -CH(R)N(R)C(O)O-, -CH(R)S(O)N(R)-, -CH(R)S(O)2N(R)-, -CH(R)N[C(O)R]S(O)-, -CH(R)N[C(O)R]S(O)2-, -CH(R)N(R)S(O)N(R)-, -CH(R)N(R)S(O)2N(R)-, -CH(R)C(O)N(R)C(O)-, -CH(R)S(O)N(R)C(O)-, -CH(R)S(O)2N(R)C(O)-, -CH(R)OS(O)N(R)-, -CH(R)OS(O)2N(R)-, -CH(R)N(R)S(O)O-, -CH(R)N(R)S(O)2O-, -CH(R)N(R)S(O)C(O)-, -CH(R)N(R)S(O)2C(O)-, -CH(R)SON[C(O)R]-, -CH(R)S(O)2N[C(O)R]-, -CH(R)N(R)SON(R)-, -CH(R)N(R)S(O)2N(R)-; -CH(R)C(O)O-, -CH(R)N(R)P(OR')O-, -CH(R)N(R)P(OR')-, -CH(R)N(R)P(O)(OR')O-, -CH(R)N(R)P(O)(OR')-, -CH(R)N[C(O)R]P(OR')O-, -CH(R)N[C(O)R]P(OR')-, -CH(R)N[C(O)R]P(O)(OR')O- or -CH(R)N[C(O)R]P(OR')-. In L, each R and R' is, independently, -H, acyl, substituted or unsubstituted aliphatic, aromatic, arylalkyl, heteroarom., cycloalkyl or arylalkyl; or L is -RbN(R)S(O)2-, -RbN(R)P(O)-, or -RbN(R)P(O)O-, wherein Rb is an alkylene group which when taken together with the sulfonamide, phosphinamide, or phosphonamide group to which it is bound forms a five or six membered ring fused to ring A; or L is II (X = O or nil; Y = O or nil) or III (Y = O, nil) wherein R85 taken together with the phosphinamide, or phosphonamide is a 5-, 6-, or 7-membered, aromatic, heteroarom. or heterocycloalkyl ring system. G is a direct bond, -(CH2)j- (j = 1-6), C2-C6-alkenylene, C3-C8-cycloalkylene or C1-C6-oxaalkylene group. R1 is substituted or optionally substituted aliphatic, cycloalkyl, bicycloalkyl, cycloalkenyl, aromatic, heteroarom., heteroaralkyl, heterocycloalkyl, heterobicycloalkyl, alkylamido, arylamido, -S(O)2-alkyl, -S(O)2-cycloalkyl, -C(O)alkyl, or -B-E, wherein B is substituted or unsubstituted cycloalkyl, heterocycloalkyl, aromatic, heteroarom., alkylene, aminoalkyl, alkylenecarbonyl, or aminoalkylcarbonyl and E is substituted or unsubstituted azacycloalkyl, azacycloalkylcarbonyl, azacycloalkylsulfonyl, azacycloalkylalkyl, heteroaryl, heteroarylcarbonyl, heteroarylsulfonyl, heteroaralkyl, alkyl sulfonamido, aryl sulfonamido, bicycloalkyl, ureido, thioureido or aryl. R2 is -H or substituted or unsubstituted aliphatic, cycloalkyl, halogen, -OH, cyano, aromatic, heteroarom., heterocycloalkyl, aralkyl, heteroaralkyl, -(CH2)0-3NR4R5, or -(CH2)0-3C(O)NR4R5. R3 is substituted or unsubstituted aliphatic, alkenyl, cycloalkyl, aromatic, heteroarom., or heterocycloalkyl with provisos. R4, R5 and the N atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, heterobicycloalkyl or heteroarom.; or R4 and R5 are each, independently, -H, azabicycloalkyl, heterocycloalkyl, substituted or unsubstituted alkyl or Y-Z; Y is -C(O)-, -(CH2)p-, -S(O)2-, -C(O)O-, -SO2NH-, -CONH-, -(CH2)pO-, -(CH2)pNH-, -(CH2)pS-, -(CH2)pS(O)-, and -(CH2)pS(O)2-; p = 0-6; and Z is -H, or substituted or unsubstituted alkyl, amino, aryl, heteroaryl or heterocycloalkyl. 546 Example prepns. are included. For example, addition of piperidine to 4-[4-amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]cyclohexanone in DCE and AcOH, followed by treatment with Na[(AcO)3BH], workup and chromatog., gave cis- and trans-IV.

2001:730744 Document Number 135:288790 Pyrrolopyrimidines as tyrosine kinase inhibitors. Hirst, Gavin C.; Calderwood, David; Munschauer, Rainer; Arnold, Lee D.; Johnston, David N.; Rafferty, Paul (Basf Aktiengesellschaft, Germany). PCT Int. Appl. WO 2001072751 A1 20011004, 453 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US8593

20000329.

IT **Multiple sclerosis**
(therapeutic agents; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 262442-50-2P 262442-56-8P 262442-76-2P 262442-90-0P 364353-91-3P
364353-94-6P 364353-96-8P 364354-00-7P 364354-01-8P
364354-05-2P 364354-08-5P 364354-14-3P 364354-16-5P 364354-17-6P
364354-19-8P 364354-21-2P 364354-26-7P 364354-27-8P 364354-28-9P
364354-30-3P 364354-32-5P 364354-34-7P 364354-36-9P 364354-39-2P
364354-40-5P 364354-41-6P 364354-42-7P 364354-43-8P 364354-44-9P
364354-45-0P 364354-46-1P 364354-47-2P 364354-48-3P 364354-51-8P
364354-52-9P 364354-53-0P 364354-54-1P 364354-55-2P 364354-56-3P
364354-57-4P 364354-59-6P 364354-60-9P 364354-61-0P 364354-62-1P
364354-63-2P 364354-64-3P 364354-65-4P 364354-66-5P 364354-68-7P
364354-69-8P 364354-70-1P 364354-71-2P 364354-72-3P 364354-73-4P
364354-74-5P 364354-75-6P 364354-80-3P 364354-81-4P 364354-85-8P
364354-86-9P 364354-90-5P 364354-94-9P 364354-95-0P 364354-97-2P,
Cis-4-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-[2-[(1H-imidazol-2-ylmethyl)amino]ethyl]-1-cyclohexanol diacetate
364354-98-3P 364354-99-4P 364355-00-0P 364355-01-1P 364355-02-2P
364355-03-3P 364355-04-4P 364355-06-6P, Trans-1-(Aminomethyl)-4-[4-amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-cyclohexanol diacetate 364355-07-7P 364355-08-8P 364355-09-9P 364355-10-2P
364355-11-3P 364355-12-4P 364355-13-5P 364355-14-6P 364355-15-7P
364355-16-8P 364355-18-0P 364355-19-1P 364355-20-4P 364355-21-5P
364355-22-6P 364355-23-7P 364355-24-8P 364355-25-9P 364355-27-1P,
Cis-8-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1,3-diazaspiro[4.5]decan-2-one 364355-29-3P, Cis-4-[4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-1-ammoniocyclohexylmethanol acetate 364355-33-9P 364355-35-1P
364355-38-4P, 5-[4-(Benzyloxy)phenyl]-7-(1,4-dioxaspiro[4.5]dec-8-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine 364355-40-8P 364355-41-9P
364355-44-2P 364355-51-1P 364355-53-3P 364355-56-6P 364355-57-7P
364355-58-8P 364355-59-9P 364355-60-2P 364355-62-4P 364355-63-5P
364355-64-6P 364355-65-7P 364355-66-8P 364355-68-0P 364355-71-5P
364355-75-9P 364355-76-0P 364355-77-1P 364355-78-2P 364355-79-3P
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364355-85-1P 364355-86-2P 364355-87-3P 364355-88-4P 364355-89-5P
364355-90-8P 364355-91-9P 364355-92-0P 364355-93-1P 364355-96-4P
364355-97-5P 364356-05-8P 364356-08-1P 364356-11-6P 364356-13-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 62-53-3, Aniline, reactions 75-64-9, tert-Butylamine, reactions
77-86-1 78-96-6, 1-Amino-2-propanol 79-30-1, Isobutyryl chloride
96-20-8, 2-Amino-1-butanol 98-09-9, Benzenesulfonyl chloride 98-80-6, Phenylboronic acid 100-36-7, N,N-Diethylethylenediamine 100-52-7, Benzaldehyde, reactions 100-55-0, 3-Pyridylmethanol 103-71-9, Phenyl isocyanate, reactions 103-80-0, Phenacetyl chloride 104-78-9, 3-Diethylaminopropylamine 105-36-2, Ethyl bromoacetate 105-83-9
108-00-9, N,N-Dimethylethylenediamine 108-15-6, 1-Dimethylamino-2-propylamine 109-01-3, N-Methylpiperazine 109-02-4, 4-Methylmorpholine
109-55-7 109-85-3, 2-Methoxyethylamine 110-89-4, Piperidine, reactions
110-91-8, Morpholine, reactions 115-69-5, 2-Amino-2-methyl-1,3-propanediol 120-29-6, Tropine 120-43-4, Ethyl 1-piperazinecarboxylate
121-05-1, N,N-Diisopropylethylenediamine 123-00-2, 4-(3-

Aminopropyl)morpholine 123-75-1, Pyrrolidine, reactions 124-68-5 140-31-8, 2-(Piperazin-1-yl)ethylamine 142-25-6, N,N,N'-Trimethylethylenediamine 156-87-6, 3-Amino-1-propanol 285-69-8, 3,6-Dioxabicyclo[3.1.0]hexane 288-32-4, Imidazole, reactions 349-88-2, 4-Fluorobenzenesulfonyl chloride 364-73-8, 5-Bromo-2-fluoronitrobenzene 367-24-8, 4-Bromo-2-fluoroaniline 446-52-6, 2-Fluorobenzaldehyde 453-20-3, Tetrahydro-3-furanol 501-53-1, Benzyl chloroformate 535-11-5, Ethyl 2-bromopropionate 540-38-5, 4-Iodophenol 574-98-1 586-95-8, 4-Pyridylmethanol 586-98-1, 2-Pyridylmethanol 615-18-9, 2-Chlorobenzoxazole 616-30-8, 3-Amino-1,2-propanediol 622-40-2, 2-Morpholinoethanol 623-04-1, 4-Aminobenzyl alcohol 645-45-4, Hydrocinnamoyl chloride 929-06-6, 2-(2-Aminoethoxy)ethanol 1445-73-4, 1-Methylpiperid-4-one 1765-93-1, 4-Fluorophenylboronic acid 1878-68-8, 4-Bromophenylacetic acid 1885-14-9, Phenyl chloroformate 2038-03-1, 4-(2-Aminoethyl)morpholine 2081-44-9, Tetrahydro-2H-4-pyranol 2105-94-4, 4-Bromo-2-fluorophenol 2295-31-0, 2,4-Thiazolidinedione 2362-12-1, 4-Bromo-2-methylphenol 2706-56-1, 2-(2-Aminoethyl)pyridine 2749-11-3, (S)-(+)-2-Amino-1-propanol 2799-16-8 2799-21-5, (R)-(+)-3-Pyrrolidinol 2969-81-5, Ethyl 4-bromobutyrate 3173-56-6, Benzyl isocyanate 3282-30-2, 2,2-Dimethylpropanoyl chloride 3529-08-6, 1-Piperidinepropanamine 3586-14-9, 3-Phenoxytoluene 3964-56-5, 4-Bromo-2-chlorophenol 4097-89-6 4318-37-0, N-Methylhomopiperazine 4524-93-0, Cyclopentanecarbonyl chloride 4530-20-5, N-(tert-Butoxycarbonyl)glycine 4727-72-4, 1-Benzyl-4-hydroxypiperidine 4746-97-8, 1,4-Dioxaspiro[4.5]decan-8-one 4892-89-1, 1-(2-Morpholinoethyl)piperazine 5036-48-6, N-(3-Aminopropyl)imidazole 5382-16-1, 4-Hydroxypiperidine 5464-28-8, 1,3-Dioxolane-4-methanol 6168-72-5 6602-54-6, 2-Chloronicotinonitrile 6850-38-0, 2-Aminocyclohexanol 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 7368-78-7, 4-Bromoguaiacol 7462-74-0, 2-Bromo-2-methylpropanamide 7663-77-6, 1-(3-Aminopropyl)-2-pyrrolidinone 10111-08-7, 1H-Imidazole-2-carboxaldehyde 10221-56-4 10316-79-7, 1-Amino-1-cyclopentanemethanol 13552-21-1, 1-Amino-2-butanol 13694-84-3 16369-05-4, 2-Amino-3-methyl-1-butanol 17082-09-6, (E)-Cinnamoyl chloride 17342-08-4 17702-83-9, N-(8-Bromooctyl)phthalimide 18853-55-9 19764-58-0, N2,N2-Dimethyl-1,2-propanediamine 20173-24-4, 3-(2-Aminoethyl)pyridine 20412-38-8, Neopentyl chloroformate 22795-97-7 23159-07-1, 1-Pyrrolidinepropanamine 23356-96-9, (S)-(+)-2-Pyrrolidinemethanol 23511-05-9 24304-84-5, 2-((2-Aminoethyl)thio)ethanol 26116-12-1, 2-(Aminomethyl)-1-ethylpyrrolidine 26177-44-6, 4-Bromobenzylamine hydrochloride 26394-17-2, Cyclopentanesulfonyl chloride 27578-60-5, 1-(2-Aminoethyl)piperidine 28179-33-1, 2-Bromo-4'-phenoxyacetophenone 34610-36-1 35166-33-7, (5-Methyl-3-isoxazolyl)methanol 39890-46-5 39901-94-5, 2-Pyridinecarbonyl chloride hydrochloride 40499-83-0, Pyrrolidin-3-ol 50893-53-3, α-Chloroethyl chloroformate 51067-38-0, 4-Phenoxyphenylboronic acid 53369-71-4, N,N-Dimethylneopentanediamine 55458-67-8, 1,3-Dimethyl-5-pyrazolecarbonyl chloride 56344-32-2, N-(3-Hydroxypropyl)ethylenediamine 61278-21-5, 1,2-Propanediol, 3-amino-, (S)- 64248-64-2, 2,5-Difluorobenzonitrile 66211-46-9 79099-07-3, N-tert-Butoxycarbonyl-4-piperidone 82417-45-6, 2,3-Dichlorobenzenesulfonyl chloride 86087-23-2, (S)-3-Hydroxytetrahydrofuran 93777-26-5, 5-Bromo-2-fluorobenzaldehyde 97986-34-0 105942-08-3, 4-Bromo-2-fluorobenzonitrile 113451-59-5 116183-82-5, (3R)-(+)-3-Aminopyrrolidine 123148-78-7 132958-72-6, (3R)-(+)-3-(Dimethylamino)pyrrolidine 137049-00-4, 1-Methylimidazole-4-sulfonyl chloride 146631-00-7, 4-(Benzyloxy)phenylboronic acid

195046-28-7 213743-76-1 213744-35-5 262433-02-3 262433-41-0
262433-42-1 262433-49-8 262442-03-5 262442-79-5 262444-52-0
262444-53-1 262444-54-2 **262444-55-3** 262444-56-4
262444-57-5 262444-58-6 262444-59-7 262444-60-0 262444-61-1
262444-62-2 262444-63-3 262444-65-5 330794-10-0 364354-29-0,
7-(1-Oxaspiro[2.5]oct-6-yl)-5-(4-phenoxyphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine 364354-33-6 364354-35-8 364355-50-0 364355-52-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

IT 262431-69-6P 262433-52-3P 262439-86-1P 262439-87-2P 262439-88-3P
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262440-11-9P **262440-12-0P** 262440-13-1P 262440-14-2P
262440-15-3P 262440-16-4P 262440-17-5P **262440-18-6P**
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262442-59-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of pyrrolopyrimidinamines as protein kinase inhibitors)

L5 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
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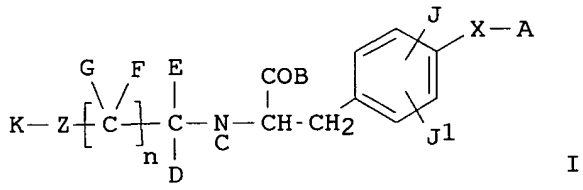

I

AB Phenylalanine derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof [wherein X represents an interat. bond, O, OSO2, N-(un)substituted NH, NHCO, NHSO2, NHCONH, or NH(CS)NH, CO; Y and Z represent each CO, SO, or SO2; A represents a specific substituted Ph group or nitrogen-containing heterocycle such as aromatic-fused pyrimidinedione or pyrimidinone, 2,4- or 2,5-imidazolidinedione, or 5-imidazolone; C represents hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl; D and E represent each lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or D and E may be bonded to each other to form a ring optionally containing 1 or 2 O, N, or S in the ring; F and G represent each hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or F and G may be bonded to each other to form a ring; n is from 0 to 2; K represents OR7, NR7R8, NHNR7R8, SR7, or R7; R7 and R8 represents H, lower alkyl, etc.; and J and J' represent each hydrogen, halogeno, lower alkyl, lower alkoxy, or NO2] are prepared These derivs. and analogs thereof show an α4 integrin inhibitory activity and are usable as remedies for various diseases relating to α4 integrin, such as inflammatory diseases related to α4 integrin-dependent adhesion process, arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, **multiple sclerosis**, Sjoegren syndrome, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, O-(2,6-dichlorobenzyl)-L-tyrosine bound to Wang resin was allowed to react with diethylmalonic acid, HOAt, 2-dimethylaminoisopropyl chloride hydrochloride (DIC), and N-methyl-2-pyrrolidinone (NMP) at room temperature for 16 h, washed with DMF five times, and condensed with pyrroline using HOAt, DIC, and NMP, followed by oxidation with OsO4 in dioxane at room temperature for 16
and resin-cleavage in aqueous CF3CO2H to give N-[2-[(cis-2,4-dihydroxypyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-O-(2,6-dichlorobenzyl)-L-tyrosine (II). II and N-[2-[(pyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-

4-(2,6-dichlorobenzoylamino)-L-phenylalanine inhibited the binding of human recombinant VCAM-1 to human B lymphoma cell line expressing integrin$\alpha 4\beta 7$ with IC50 of ≤ 0.02 μmol/L.

2001:380546 Document Number 134:367194 Preparation of novel phenylalanine derivatives as α4-integrin inhibitors. Tanaka, Yasuhiro; Yoshimura, Toshihiko; Izawa, Hiroyuki; Ejima, Chieko; Kojima, Mitsuhiko; Atake, Yuko; Nakanishi, Eiji; Suzuki, Nobuyasu; Makino, Shingo; Suzuki, Manabu; Murata, Masahiro (Ajinomoto Co., Inc., Japan). PCT Int. Appl. WO 2001036376 A1 20010525, 155 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP8152 20001120. PRIORITY: JP 1999-328468 19991118; JP 2000-197139 20000629.

AB . . . to α4 integrin, such as inflammatory diseases related to α4 integrin-dependent adhesion process, arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, **multiple sclerosis**, Sjoegren syndrome, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, O-(2,6-dichlorobenzyl)-L-tyrosine bound to. . .

ST . . . integrin inhibitor; inflammatory disease treatment phenylalanine deriv prepn; arthritis treatment phenylalanine deriv prepn; systemic lupus erythematosus treatment phenylalanine deriv prepn; **multiple sclerosis** treatment phenylalanine deriv prepn; Sjoegren syndrome treatment phenylalanine deriv prepn; psoriasis treatment phenylalanine deriv prepn; allergy treatment phenylalanine deriv prepn;. . .

IT Allergy inhibitors
Antiarteriosclerotics
Antiarthritics
Antidiabetic agents
Antitumor agents
Cardiovascular agents
Multiple sclerosis
Psoriasis
Sjogren's syndrome
(preparation of novel phenylalanine derivs. as α4-integrin inhibitors)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel phenylalanine derivs. as α4-integrin inhibitors)

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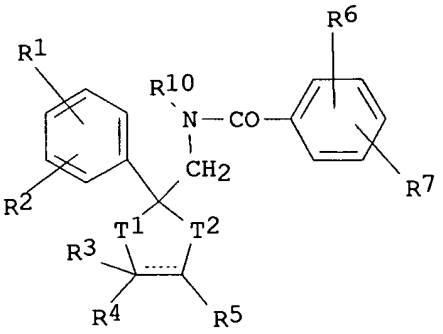

I

AB The title compds. I [T1 = (CH2)x; T2 = (CH2)y; dotted line indicates a single bond or double bond; x, y = 0 - 2; R1, R2, R6, R7 = halo, hydroxy,

alkyl, etc.; R3, R4 = H, cyano, nitro, etc.; further details on R3 and R4 are given; R5 = H, halo, hydroxy, etc.; further details on R3 and R5 are given; R10 = H, etc.], useful as potassium channel inhibitors (no data), are prepared I are useful in the treatment of autoimmune disorders, cardiac arrhythmias (no data), etc. Formulations are given.

2000:314533 Document Number 132:334285 Preparation of phenyloxoazapropylcycloalkane derivatives and analogs as potassium channel inhibitors. Baker, Robert K.; Chee, Jennifer; Bao, Jianming; Garcia, Maria L.; Kaczorowski, Gregory J.; Kotliar, Andrew; Kayser, Frank; Liu, Chou Juitsai; Miao, Shouwu; Rupprecht, Kathleen M.; Parsons, William H.; Schmalhofer, William A.; Claiborne, Christopher F.; Liverton, Nigel; Claremon, David A.; Thompson, Wayne J. (Merck & Co., Inc., USA). PCT Int. Appl. WO 2000025770 A1 20000511, 243 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US24949 19991026. PRIORITY: US 1998-PV106416 19981030.

IT **Encephalomyelitis**
(autoimmune; preparation and effect of phenyloxoazapropylcycloalkane derivs. and analogs with potassium channel inhibiting activity)

IT Diabetes mellitus
Multiple sclerosis
Myasthenia gravis
Rheumatoid arthritis
Transplant and Transplantation
(preparation and effect of phenyloxoazapropylcycloalkane derivs. and analogs with potassium channel inhibiting activity)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and effect of phenyloxoazapropylcycloalkane derivs. and analogs with potassium channel inhibiting activity)

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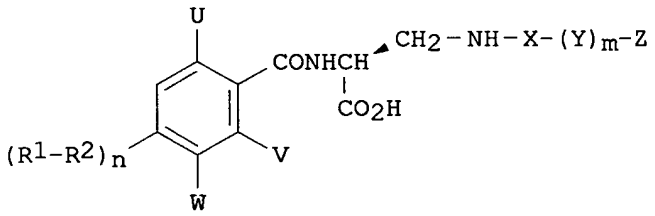

I

AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepared and are useful for treating rheumatoid

arthritis, psoriasis, **multiple sclerosis**, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute myocardial infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepared by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-associated antigen-1)/ICAM-1 protein-protein assay.

2000:260225 Document Number 132:294010 Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors. Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya (F. Hoffmann-La Roche A.-G., Switz.). PCT Int. Appl. WO 2000021920 A1 20000420, 259 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP7620 19991012. PRIORITY: US 1998-PV104120 19981013.

AB . . . = 0, 1] or their pharmaceutically acceptable salts or esters were prepared and are useful for treating rheumatoid arthritis, psoriasis, **multiple sclerosis**, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute. . .

IT Anti-inflammatory agents
Atherosclerosis
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

IT

245463-44-9P	245463-46-1P	245463-47-2P	245463-49-4P	245463-50-7P
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264275-54-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

L5 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Peptides R1NR2XCONR4CR52CONHY [Y = CH(CHO)CH2(CH2)mCOR7, (m = 0 or 1 and R7 = OH or ester, NHOH) or cyclic lactol derivative when R7 is OH; X = CR32 or NR3 (R3 = H, an amino acid side chain, alkyl, cycloalkyl, aryl, etc.); R1 = H, R8, COR8, COCOR8, SO2R8, SOR8, CO2R8, CONHR8, SO2NHR8, SONHR8, COCONHR8, COCH:CHR8, etc. (R8 = alkyl, cycloalkyl, aryl, etc.); R2 = H or R2 and R3 may form a ring; R4 = H and R5 = H, amino acid side chain, R8, etc. or R4 and R5 may form a ring] were prepared as inhibitors of caspases. Thus, p-AcNHC6H4CO-L-Val-L-Pro-NHCH(CHO)CH2CO2H-(S) was prepared by the solid-phase method and showed ki < 10 nm for inhibition of interleukin-1β converting enzyme (ICE, caspase-1).
1999:613942 Document Number 131:243593 Preparation of peptides as inhibitors of caspases. Wannamaker, Marion W.; Bemis, Guy W.; Charifson, Paul S.; Lauffer, David J.; Mullican, Michael D.; Murcko, Mark A.; Wilson, Keith P.; Janetka, James W.; Davies, Robert J.; Grillot, Anne-Laure; Shi, Zhan; Forster, Cornelia J. (Vertex Pharmaceuticals Incorporated, USA). PCT Int. Appl. WO 9947545 A2 19990923, 297 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US5919 19990319. PRIORITY: US 1998-PV78770 19980319.

IT Aging, animal
Alcoholism
Alopecia
Alzheimer's disease
Anti-inflammatory agents
Antiasthmatics
Antiviral agents
Apoptosis
Autoimmune disease
Bone, disease
Encephalitis
Graves' disease
Leukemia
Lupus erythematosus
Multiple myeloma
Multiple sclerosis
Myasthenia gravis
Myelodysplastic syndromes
Osteoarthritis
Osteoporosis
Parkinson's disease
Psoriasis
Rheumatoid arthritis
Sepsis
Spinal muscular atrophy
Transplant rejection
(preparation of peptides as inhibitors of caspases)

IT

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244134-55-2P 244134-58-5P 244134-59-6P 244134-60-9P 244134-61-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as inhibitors of caspases)

L5 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [one of X, X1 = H, halo, lower alkyl and the other = (un)substituted group X6, X7, X10; R1 = H, lower alkyl; n = 0, 1; Het = 5-6 membered heteroarom. ring containing 1-3 heteroatoms N, O, S, or 9-10 membered bicyclic heteroarom. ring containing 1-4 heteroatoms N, O, S; R19 = (un)substituted lower alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl; R18 = H, any group R19; R20 = (un)substituted lower alkyl, aroyl, lower alkanoyl; Y = CR22R23R24, 3-7 membered ring Y2; R22, R23 = (un)substituted aryl, heteroaryl, lower alkyl; R24 = H, CN, (un)substituted aryl, lower alkyl, with provisos; R25 = lower alkyl, F-(un)substituted lower alkenyl, R26(CH2)m; R26 = aryl, heteroaryl, N3, CN, OH, NO2, amino, lower alkoxy, lower alkoxycarbonyl, lower alkanoyl, lower alkylthio, lower alkylsulfonyl, lower alkylsulfinyl, etc.; Q = bond, (CH2)pO, (CH2)pS, (CH2)p; m = 0-4; p = 0-3; Z = H, lower alkyl] and pharmaceutically acceptable salts and esters thereof, are disclosed which have activity as inhibitors of binding between VCAM-1 and cells expressing integrin VLA-4. Such compds. are useful for treating diseases whose symptoms and /or damage are related to the binding of VCAM-1 to cells expressing VLA-4. Thus, amidation of 4-amino-N-[(1-phenylcyclopentyl)carbonyl]-L-phenylalanine Me ester (preparation given) with 4-quinolinecarboxylic acid and saponification gave desired title derivative II as its sodium salt. II inhibited
VLA-4 binding to immobilized VCAM-1 with IC50 = 2.7 nM in solid-phase dual antibody assay.
1999:166589 Document Number 130:209978 Preparation of N-aroylphenylalanine derivatives as vascular cell adhesion molecule-1 (VCAM-1) binding inhibitors. Chen, Li; Guthrie, Robert William; Huang, Tai-Nang; Hull, Kenneth G.; Sidduri, Achytharao; Tilley, Jefferson Wright (F.Hoffmann-La

Roche A.-G., Switz.). PCT Int. Appl. WO 9910313 A1 19990304, 215 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP5144 19980813. PRIORITY: US 1997-56929 19970822.

IT **Multiple sclerosis**
(therapeutic agents, inhibitors; preparation of N-aroylphenylalanine derivs. as vascular cell adhesion mol.-1 (VCAM-1) binding inhibitors)

IT 220876-24-4P 220876-25-5P 220876-32-4P **220876-36-8P**
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aroylphenylalanine derivs. as vascular cell adhesion mol.-1 (VCAM-1) binding inhibitors)

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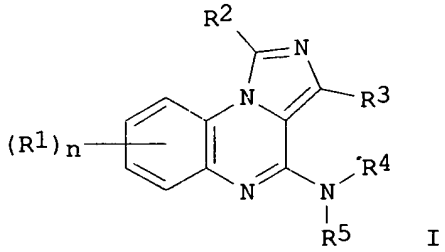
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aroylphenylalanine derivs. as vascular cell adhesion mol.-1 (VCAM-1) binding inhibitors)

L5 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



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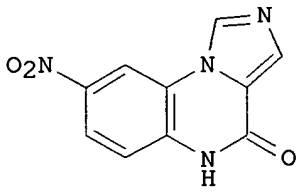

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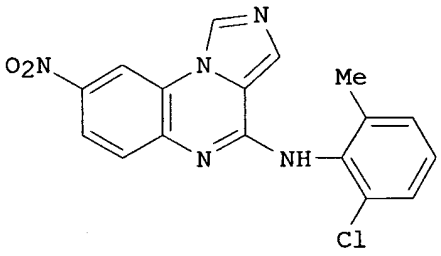

III

AB Novel imidazoquinoxalines I and salts thereof are disclosed [wherein: n = 0-4; R1, R2, R3 = H, R6, OH, OR6, SH, SR6, CO2H, SO3H, halo, cyano, NO2, etc.; R1-R3 may form ring(s); R4, R5 = H, R6, COR6; or NR4R5 forms (un)substituted 3- to 8-membered heterocyclic ring; R6 = (un)substituted alk(en/yn)yl, cycloalk(en)yl(alkyl), aryl, aralkyl, heterocyclo(alkyl)]. Also disclosed are pharmaceutical compns. containing the compds., and methods of their use in the treatment of various protein tyrosine kinase-associated disorders, such as immunol. disorders (no data). Over 500 synthetic examples are given. For instance, the nitroimidazoloquinoxalinone II (prepared in 4 steps) was treated with POCl3 to give 78% of the corresponding chloro compound, which reacted with NaN(SiMe3)2 and 2-chloro-6-methylaniline in THF to give 86% title compound III.

1999:166498 Document Number 130:223295 Preparation of imidazoquinoxaline protein tyrosine kinase inhibitors. Barrish, Joel C.; Chen, Ping; Das, Jagabandhu; Iwanowicz, Edwin J.; Norris, Derek J.; Padmanabha, Ramesh; Roberge, Jacques Y.; Schieven, Gary L. (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 9909845 A1 19990304, 315 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US16027 19980803. PRIORITY: US 1997-56770 19970825; US 1997-69159 19971209.

IT Ischemia
Lupus erythematosus
Multiple sclerosis
Psoriasis
Transplant rejection
(treatment; preparation of imidazoquinoxalines as protein tyrosine kinase inhibitors)

IT

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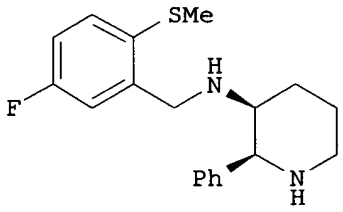
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of imidazoquinoxalines as protein tyrosine kinase inhibitors)

L5 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



II

AB Title compds. R1A(W)CH2NR2R3 (I) are claimed [wherein A = benzene, naphthalene, thiophene, dihydroquinoline, or indoline nucleus (amine-bearing sidechain is attached to a ring C atom); W = H, alkyl, alkylthio, halo, (fluoro)alkoxy; R1 = (un)substituted amino, alkyl- or arylthio, -sulfinyl, or -sulfonyl, aryloxy, etc.; R2 = H, alkoxycarbonyl; R3 = various N-containing aliphatic mono-, bi-, and polycyclic systems, attached at a C atom], as well as their pharmaceutically acceptable salts. I are substance P receptor antagonists (no data), useful as antiinflammatories, CNS agents, etc. Examples cover preparation of approx. 60 invention compds., 50 intermediates, plus a variety of salts and/or free bases. For example, formylation of p-FC6H4SMe with MeOCHCl2 and TiCl4 gave 5-fluoro-2-(methylthio)benzaldehyde, which underwent reductive amination with cis-3-amino-6-oxo-2-phenylpiperidine and subsequent reduction of the oxo group with BH3.THF to give title compound II.
1996:646442 Document Number 125:300828 Nonaromatic heterocycles containing substituted benzylamine nitrogen, useful as substance P receptor antagonists.. Howard, Harry R., Jr.; Ikunaka, Masaya; Ito, Fumitaka; Lowe, John A., III; Nakane, Masami; O'Neill, Brian T. (Pfizer Inc., USA). Span. ES 2087813 A1 19960716, 52 pp. (Spanish). CODEN: SPXXAD. APPLICATION: ES 1993-1771 19930809.
IT Nerve, disease
(peripheral **neuropathy**, treatment; preparation of nonarom. heterocyclic benzylamine derivs. as substance P receptor antagonists)
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nonarom. heterocyclic benzylamine derivs. as substance P receptor antagonists)

L5 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
GI For diagram(s), see printed CA Issue.
AB Title compds. I [ring A is an aryl group selected from Ph, naphthyl, thienyl, dihydroquinolinyl, indolinyl; CH2NR2R3 side chain is attached to a C atom of ring A; W = H, C1-6 alkyl, S-(C1-3) alkyl, halo, C1-6 alkoxy optionally substituted with 1-3 F atoms; R1 = a variety of amino, amido, and S(O)v-containing groups (v = 0-2), etc.; R2 = H, CO2(C1-10 alkyl); R3 = a wide variety of substituted N-containing saturated heterocycles] are prepared as

substance P receptor antagonists. The novel compds. I are useful in the treatment of inflammatory and central nervous system disorders, as well as other disorders (no data). Included are pharmaceutical compns. for use in treatment or prevention of inflammatory diseases, anxiety, colitis, depression or dysthymic disorders, psychosis, pain, allergies, chronic obstructive airways disease, hypersensitivity disorders, vasospastic diseases, fibrosing and collagen diseases, reflex sympathetic dystrophy, addiction disorders, stress related somatic disorders, peripheral **neuropathy**, neuralgia, **neuropathol**. disorders, disorders related to immune enhancement or suppression and rheumatic disease in a mammal. Some of the 62 example compds. of the invention for which the prepns. and characterization data are described include cis-3-(5-fluoro-2-methylthiobenzyl)amino-2-phenylpiperidine dihydrochloride, (+)-(2S,3S)-3-[2-methoxy-5-(N-isopropyl-N-methanesulfonylamino)benzyl]amino-2-phenylpiperidine dihydrochloride,

(1SR,2SR,3SR,4RS)-3-(2-methoxy-5-(N-methyl-N-methanesulfonylamino)benzyl)amino-2-benzhydryl-[2.2.1]azanorbornane dihydrochloride, and (2S,3S)-N-(2-methoxy-5-methylthiophenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]octan-3-amine mesylate.

1995:315540 Document Number 122:105856 Preparation of substituted benzylamino nitrogen containing non-aromatic heterocycles and their pharmaceutical compositions as substance P receptor antagonists. Howard, Harry R., Jr.; Ikunaka, Masaya; Ito, Fumitaka; Lowe, John A., III; Nakane, Masami; O'Neill, Brian T.; Rosen, Terry R.; Satake, Kunio (Pfizer Inc., USA). PCT Int. Appl. WO 9404496 A1 19940303, 94 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US4063 19930505. PRIORITY: US 1992-932392 19920819.

AB . . . airways disease, hypersensitivity disorders, vasospastic diseases, fibrosing and collagen diseases, reflex sympathetic dystrophy, addiction disorders, stress related somatic disorders, peripheral **neuropathy**, neuralgia, **neuropathol**. disorders, disorders related to immune enhancement or suppression and rheumatic disease in a mammal. Some of the 62 example compds.. . .

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RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as substance P receptor antagonist)

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elected species

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L5 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

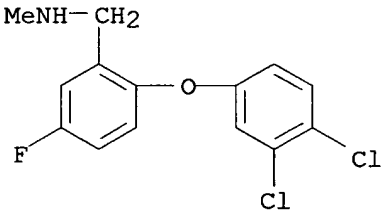
AB An osmotic pharmaceutical tablet is described which comprises a single-layer compressed core surrounded by a water permeable layer having a passageway. The single-layer core contains (i) a non-ripening drug having a solubility per dose less than about 1 mL -1 , (ii) about 2.0% to about 30% by weight of a polyethylene oxide having a weight-average, mol. weight from about 200,000 to about 7,000,000, (iii) an osmagent, and (iv) an optional disintegrant. Many osmotic tablets were prepared and their dissoln. rate were studied.

2003:678291 Document Number 139:202503 Osmotic delivery system containing a polyethylene oxide and an osmagent. Waterman, Kenneth C. (USA). U.S. Pat. Appl. Publ. US 2003161882 A1 20030828, 12 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-352258 20030127. PRIORITY: US 2002-PV353502 20020201.

IT **289716-93-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osmotic delivery system containing polyethylene oxide and osmagent)

RN 289716-93-4 HCAPLUS

CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

AB ROZCR3R4NR1R2 [R = (un)substituted Ph; R1,R2 = H, alk(en)yl, alkynyl; NR1R2 = heterocyclyl; R3,R4 = H or (fluoro)alkyl; R3R4 = (un)substituted alkylene; R2R3 = atoms to complete a heterocyclic ring; Z = (un)substituted phenylene] were prepared as monoamine reuptake inhibitors (no data). Such compds. are useful exhibit activity as serotonin, norepinephrine and dopamine reuptake inhibitors, and their pharmaceutically acceptable salts, and their use in the treatment of central nervous system and other disorders.

2002:755211 Document Number 137:262839 Preparation of phenoxybenzylamines as monoamine reuptake inhibitors for treatment of CNS disorders.. Howard, Harry R.; Schmidt, Christopher J.; Seeger, Thomas F.; Elliott, Mark L. (Pfizer, Inc., USA). U.S. Pat. Appl. Publ. US 2002143003 A1 20021003, 24 pp., Cont.-in-part of U.S. Ser. Number 529,207. (English). CODEN: USXXCO. APPLICATION: US 2001-845992 20010430. PRIORITY: US 1999-PV121313

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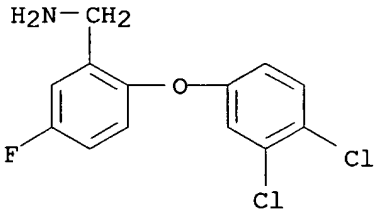
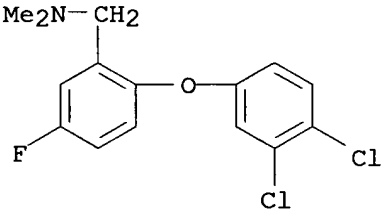
19990223; US 2000-529207 20000202; WO 2000-IB108 20000202.

IT **289716-75-2P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-
289716-92-3P, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl-, hydrochloride **289716-93-4P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, hydrochloride **289716-94-5P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- **289716-95-6P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, (2Z)-2-butenedioate (2:1) **289717-24-4P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- **289717-25-5P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (2Z)-2-butenedioate (1:1) **289717-51-7P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-, hydrochloride **289717-52-8P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- **289717-67-5P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- **289717-68-6P**, Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)-
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenoxybenzylamines as monoamine reuptake inhibitors)

RN 289716-75-2 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro- (9CI) (CA INDEX NAME)



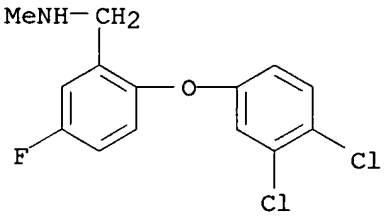
RN 289716-92-3 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

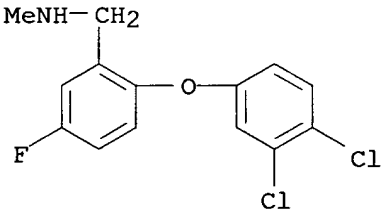
RN 289716-93-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-,

hydrochloride (9CI) (CA INDEX NAME)



● HCl

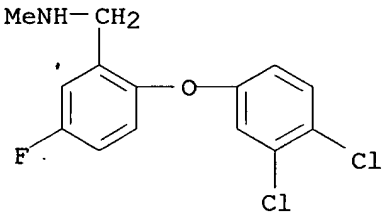
RN 289716-94-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



RN 289716-95-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

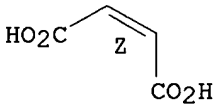
CRN 289716-94-5
CMF C14 H12 Cl2 F N O



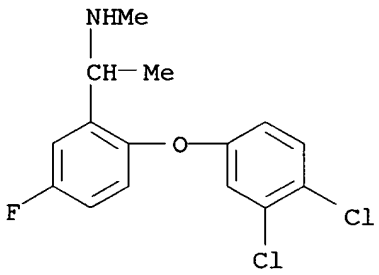
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



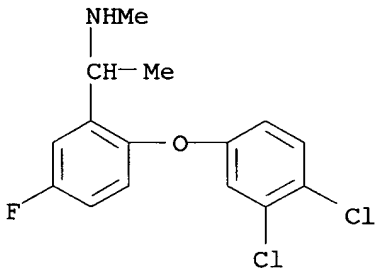
RN 289717-24-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)



RN 289717-25-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

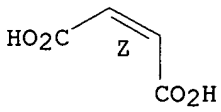
CRN 289717-24-4
CMF C15 H14 Cl2 F N O



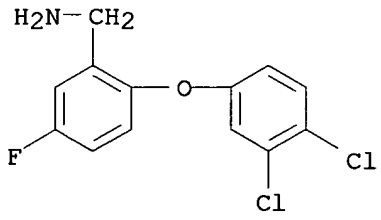
CM 2

CRN 110-16-7
CMF C4 H4 O4

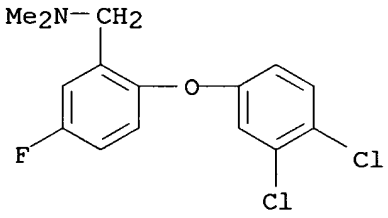
Double bond geometry as shown.



RN 289717-51-7 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-, hydrochloride (9CI) (CA INDEX NAME)

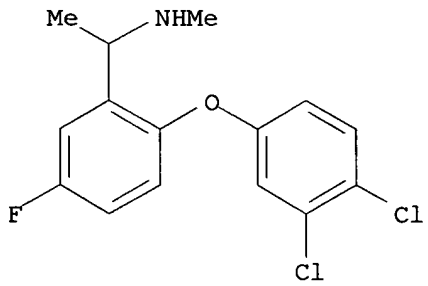


RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



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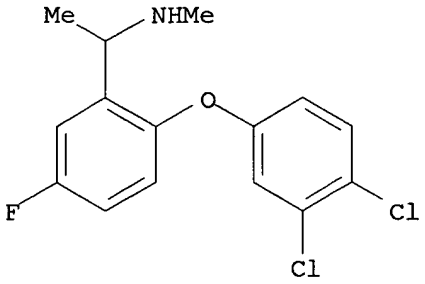
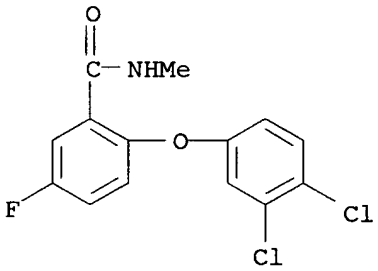
RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



IT **289718-10-1P**, Benzamide, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenoxybenzylamines as monoamine reuptake inhibitors)
RN 289718-10-1 HCAPLUS
CN Benzamide, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)

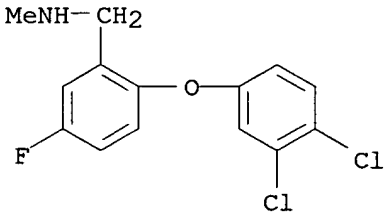


L5 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The invention provides a method for treating depression, obsessive compulsive disorder, and psychosis in a mammal, including a human, by administering to the mammal an atypical antipsychotic in combination with an antidepressant agent with improvement in efficiency. It also provides pharmaceutical compns. containing a pharmaceutically acceptable carrier, an atypical antipsychotic, and a serotonin reuptake inhibitor.
2002:674788 Document Number 137:195595 Atypical antipsychotic-antidepressant combination for treatment of depression, obsessive compulsive disorder, and psychosis. Howard, Harry R., Jr. (Pfizer Inc., USA). U.S. Pat. Appl. Publ. US 2002123490 A1 20020905, 20 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-10651 20011206. PRIORITY: US 2001-PV272619 20010301.
IT **289716-94-5 289717-24-4 289717-52-8 289717-67-5 289717-68-6 444888-21-5 444888-24-8 454456-38-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(atypical antipsychotic-antidepressant combination for treatment of depression, obsessive compulsive disorder, and psychosis)

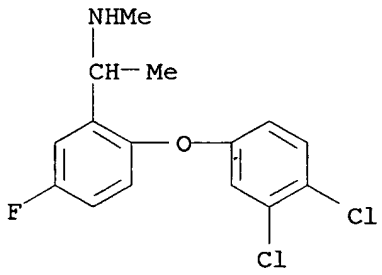
RN 289716-94-5 HCAPLUS

CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



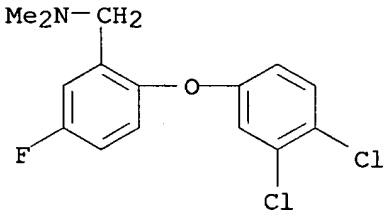
RN 289717-24-4 HCAPLUS

CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)



RN 289717-52-8 HCAPLUS

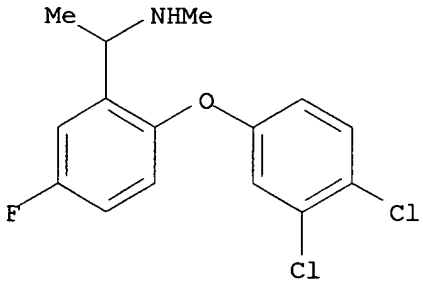
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 289717-67-5 HCAPLUS

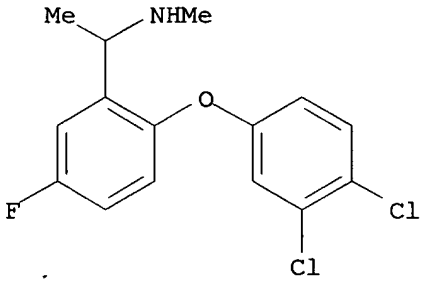
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

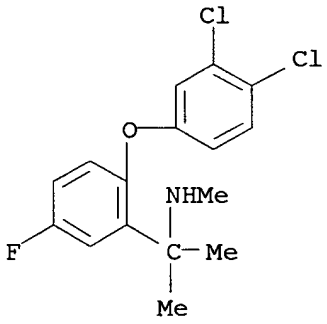


RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

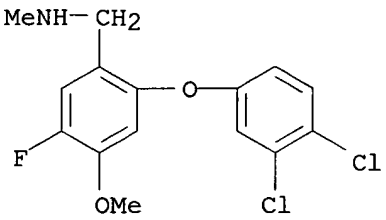
Rotation (-).



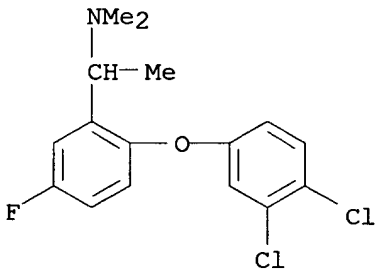
RN 444888-21-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α,α-trimethyl- (9CI) (CA INDEX NAME)



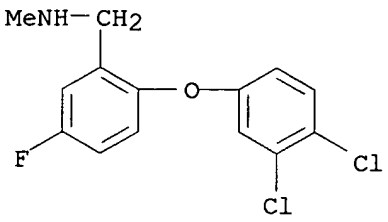
RN 444888-24-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-4-methoxy-N-methyl- (9CI) (CA INDEX NAME)



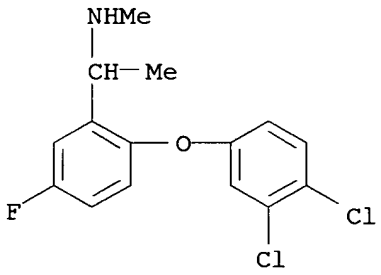
RN 454456-38-3 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N,α-trimethyl- (9CI) (CA INDEX NAME)



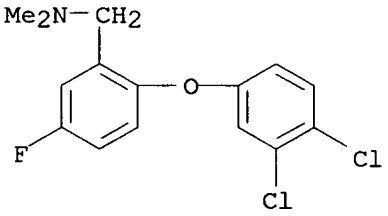
L5 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a 5-HT3 receptor antagonist in combination with a serotonin reuptake inhibitor (SRI) antidepressant agent with improvement in sexual function and/or reduction in gastro-intestinal side effects. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a 5-HT3 receptor antagonist and an SRI antidepressant. The ratio of the 5-HT3 receptor antagonist and the SRI antidepressant agent is between 0.001 to 1 and 1000 to 1, and especially between 0.01 to I and 100 to 1 (no data).
2002:595509 Document Number 137:135106 Combination of a 5-HT3 receptor antagonist with a serotonin reuptake inhibitor for the treatment of depression. Howard, Harry R. (USA). U.S. Pat. Appl. Publ. US 2002107244 A1 20020808, 20 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-2303 20011102. PRIORITY: US 2001-PV266340 20010202.
IT **289716-94-5 289717-24-4 289717-52-8 289717-67-5 289717-68-6 444888-21-5 444888-22-6 444888-24-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of 5-HT3 receptor antagonist with serotonin reuptake inhibitor for treatment of depression)
RN 289716-94-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



RN 289717-24-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)

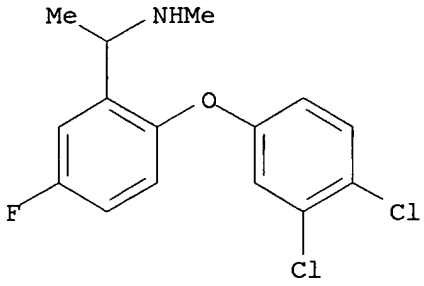


RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



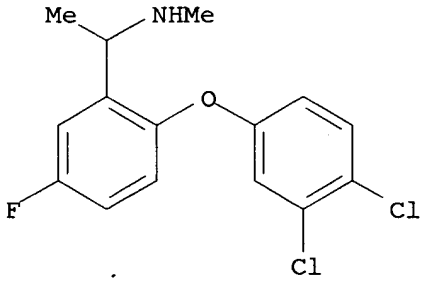
RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

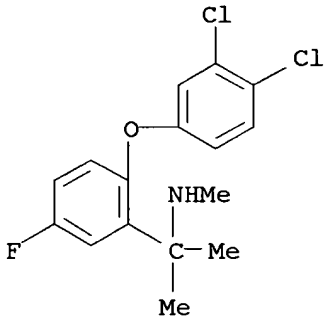


RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

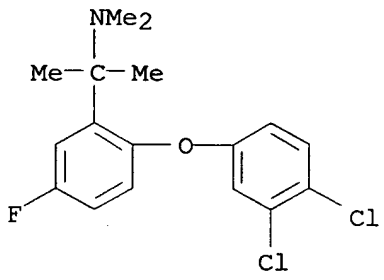
Rotation (-).



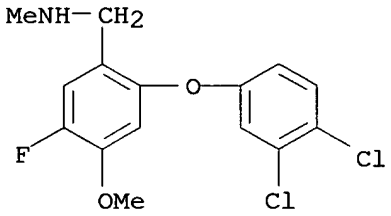
RN 444888-21-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α,α-trimethyl- (9CI) (CA INDEX NAME)



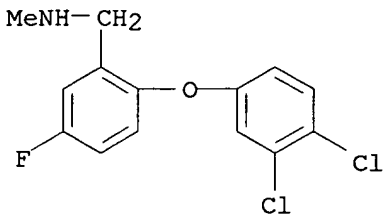
RN 444888-22-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N,α,α-tetramethyl- (9CI) (CA INDEX NAME)



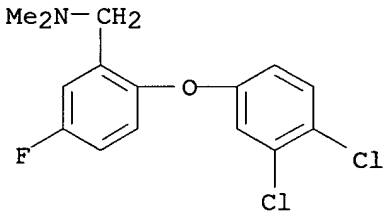
RN 444888-24-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-4-methoxy-N-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The invention provides a method of treating sleep disorders, including sleep apnea, in a mammal, including a human, by administering to the mammal a 5-HT1a antagonist or an α2-adrenergic antagonist in combination with an serotonin reuptake inhibitor (SRI) antidepressant agent with improvement in efficacy. Also provided are pharmaceutical compns. containing a pharmaceutically acceptable carrier, a 5-HT1a antagonist or an α2-adrenergic antagonist, and an SRI antidepressant agent.
2002:925264 Document Number 138:11431 5-HT1a antagonist or an α2-adrenergic antagonist in combination with an serotonin reuptake inhibitor for treatment of sleep disorders, including sleep apnea. Howard, Harry Ralph, Jr. (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1262197 A2 20021204, 22 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2002-253589 20020522. PRIORITY: US 2001-PV294322 20010530.
IT **289716-94-5 289717-52-8 289717-67-5 289717-68-6 444888-21-5 444888-22-6 444888-24-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT1a antagonist or α2-adrenergic antagonist in combination with serotonin reuptake inhibitor for treatment of sleep disorders, including sleep apnea)
RN 289716-94-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)

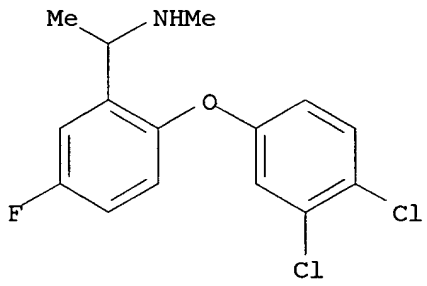


RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



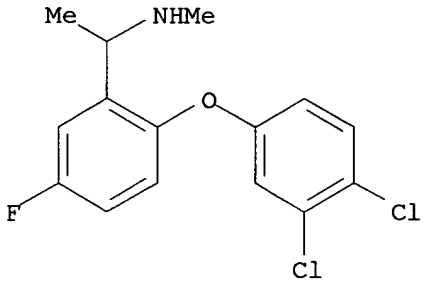
RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

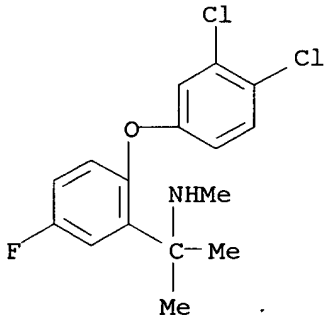


RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

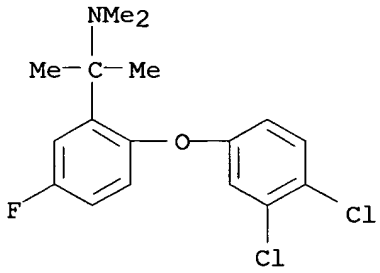
Rotation (-).



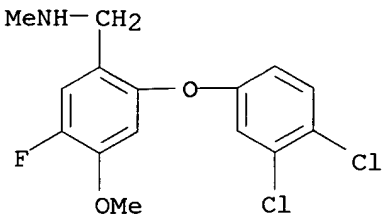
RN 444888-21-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α,α-trimethyl- (9CI) (CA INDEX NAME)



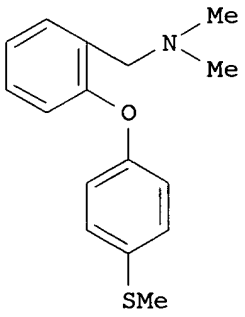
RN 444888-22-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N,α,α-tetramethyl- (9CI) (CA INDEX NAME)



RN 444888-24-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-4-methoxy-N-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
GI



I

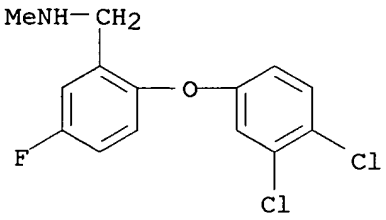
AB The present invention relates to a method of treating alcoholism or alc. dependence in a mammal, including a human, by administering to the mammal a monoamine reuptake inhibitor in combination with an opioid antagonist. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a monoamine reuptake inhibitor and an opioid antagonist. An example monoamine reuptake inhibitor is I.

2002:925263 Document Number 138:336 Combination of a monoamine reuptake inhibitor and an opioid antagonist for use in alcoholism and alcohol dependence. Howard, Harry Ralph, Jr. (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1262196 A2 20021204, 37 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2002-253105 20020502. PRIORITY: US 2001-PV293088 20010523.

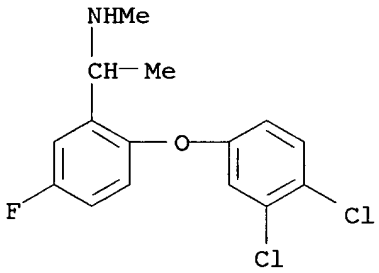
IT **289716-94-5 289717-24-4 289717-52-8 289717-67-5 289717-68-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of a monoamine reuptake inhibitor and an opioid antagonist for use in alcoholism and alc. dependence)

RN 289716-94-5 HCAPLUS

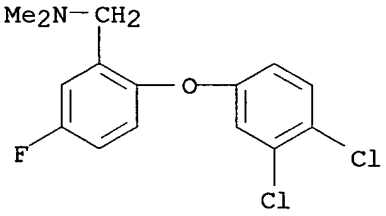
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



RN 289717-24-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)

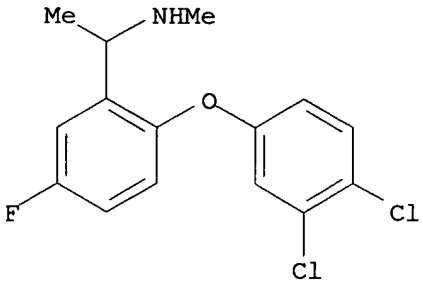


RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



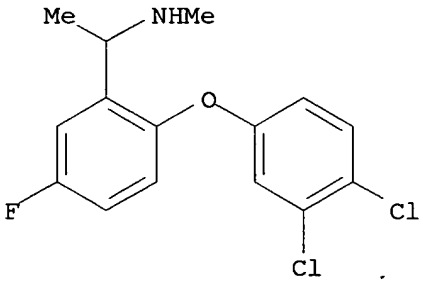
RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

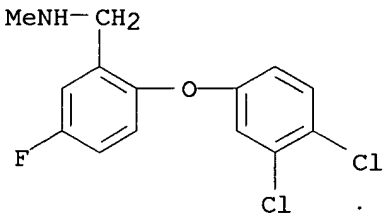


RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

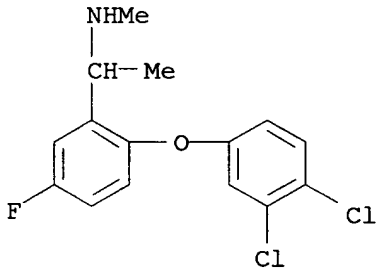
Rotation (-).



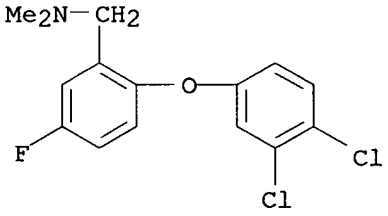
L5 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a monoamine reuptake inhibitor in combination with a dopamine D3 receptor agonist. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a monoamine reuptake inhibitor and a dopamine D3 receptor agonist.
2002:904325 Document Number 137:380038 Combination treatment with monoamine reuptake inhibitor and dopamine D3 receptor agonist for depression and anxiety. Howard, Harry Ralph, Jr. (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1260221 A2 20021127, 31 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (English). CODEN: EPXXDW. APPLICATION: EP 2002-253135 20020503. PRIORITY: US 2001-PV293063 20010523.
IT **289716-94-5 289717-24-4 289717-52-8 289717-67-5 289717-68-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoamine reuptake inhibitor; combination treatment with monoamine reuptake inhibitor and dopamine D3 receptor agonist for depression and anxiety)
RN 289716-94-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



RN 289717-24-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)

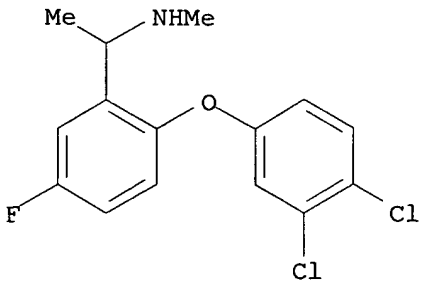


RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



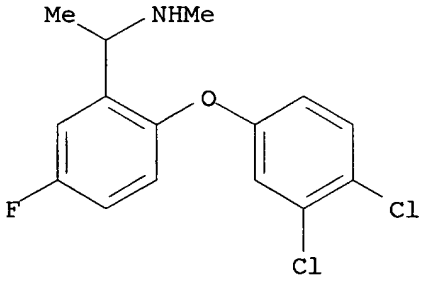
RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



L5 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
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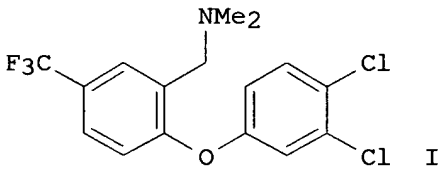


I

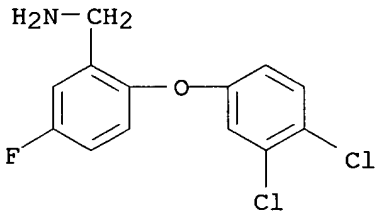
AB ROZCR3R4NR1R2 [R = (un)substituted Ph; R1,R2 = H, alk(en)yl, alkynyl; NR1R2 = heterocyclyl; R3,R4 = H or (fluoro)alkyl; R3R4 = (un)substituted alkylene; R2R3 = atoms to complete a heterocyclic ring; Z = (un)substituted phenylene] were prepared as monoamine reuptake inhibitors (no data). Thus, 2,5-F(F3C)C6H3CHO was aroxylated by 3,4-Cl2C6H3OH and the product reductively aminated by Me2NH to give title compound I.

2000:608708 Document Number 133:207665 Preparation of phenoxybenzylamines as monoamine reuptake inhibitors. Elliott, Mark Leonard; Howard, Harry Ralph, Jr.; Schmidt, Christopher Joseph; Seeger, Thomas Francis (Pfizer Products Inc., USA). PCT Int. Appl. WO 2000050380 A1 20000831, 60 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,

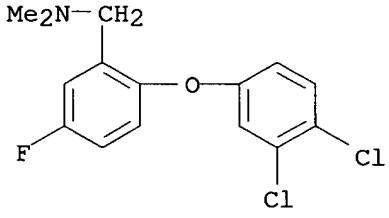
MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-IB108 20000202. PRIORITY: US 1999-PV121313 19990223.

IT **289716-75-2P 289716-92-3P 289716-93-4P**
289716-94-5P 289716-95-6P 289717-24-4P
289717-25-5P 289717-51-7P 289717-52-8P
289717-67-5P 289717-68-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenoxybenzylamines as monoamine reuptake inhibitors)

RN 289716-75-2 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro- (9CI) (CA INDEX NAME)

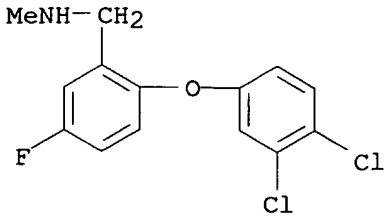


RN 289716-92-3 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



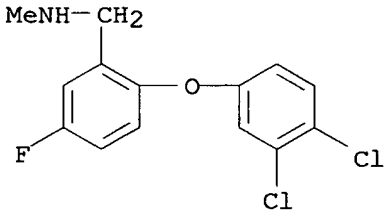
● HCl

RN 289716-93-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

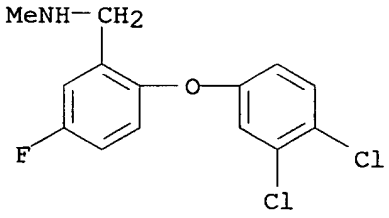
RN 289716-94-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)



RN 289716-95-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

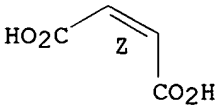
CRN 289716-94-5
CMF C14 H12 Cl2 F N O



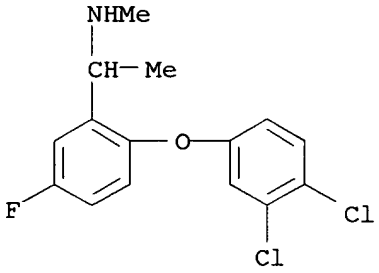
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



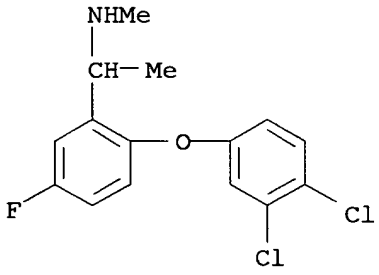
RN 289717-24-4 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl- (9CI) (CA INDEX NAME)



RN 289717-25-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

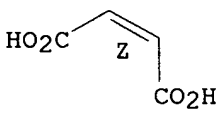
CRN 289717-24-4
CMF C15 H14 Cl2 F N O



CM 2

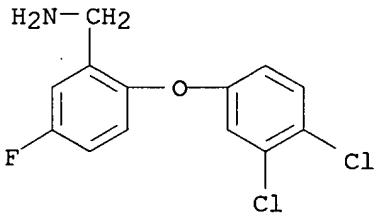
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



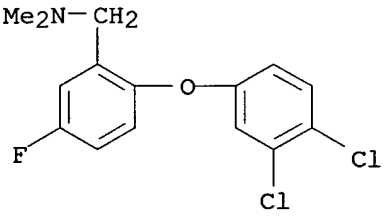
Delacroix

RN 289717-51-7 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-, hydrochloride (9CI) (CA INDEX NAME)



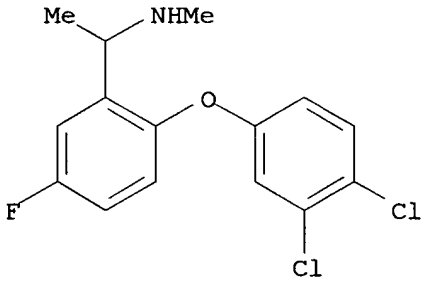
● HCl

RN 289717-52-8 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,N-dimethyl- (9CI) (CA INDEX NAME)



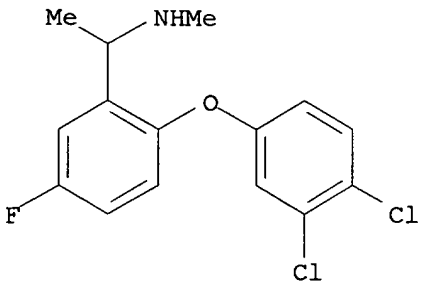
RN 289717-67-5 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 289717-68-6 HCAPLUS
CN Benzenemethanamine, 2-(3,4-dichlorophenoxy)-5-fluoro-N,α-dimethyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



IT **289718-10-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenoxybenzylamines as monoamine reuptake inhibitors)
RN 289718-10-1 HCAPLUS
CN Benzamide, 2-(3,4-dichlorophenoxy)-5-fluoro-N-methyl- (9CI) (CA INDEX NAME)